Insect Control
by
Chemicals

Insect Control by Chemicals

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CHAPTER I

Insecticides of the Mid-Twentieth Century and Their Properties

The large-scale farming practices of the twentieth century have encountered a requirement for insect control which has resulted in the rapid evolution of chemical insecticides. In the early years of this period the available materials included the arsenicals, lime-sulphur, petroleum oils, and nicotine. During the interval between World Wars I and II, the fluorine compounds were added to the inorganics, pyrethrum and rotenone were added to the botanicals, and synthetic organic materials such as the dinitro compounds and thiocyanates made their appearance. The coming of World War II witnessed the rise of the chlorinated hydrocarbon insecticides, with DDT contributed by Switzerland and BHC by the United Kingdom and France; their subsequent development in the United States was followed by the appearance of toxaphene, chlordane, aldrin, and dieldrin. Meanwhile German work during the war intro-

duced a powerful group of insecticides, the organic phosphates, among which TEPP and parathion were produced commercially in the United States, and the systemic insecticides were developed in the United Kingdom. As the century reaches the halfway mark, emphasis is returning to the eminently suitable pyrethrins, whose toxicity is being extended by admixture of the piperonyl compounds, and a synthetic analogue of which has appeared in the form of allethrin.

In this chapter, much information has been drawn from the recent publications by Frear,[44] DeOng,[34] and R. L. Metcalf.[92] Valuable background material may be obtained from the books of Martin,[84] Shepard,[107] and C. L. Metcalf and Flint,[90] published just before World War II. A number of books published in Germany during that war are listed in the bibliography of Martin and Shaw.[84a] Useful and up-to-date ancillary information is available in volumes by West and Campbell,[124] McClintock and Fisher,[87] and Isely,[70] and also recent editions of *Entoma*.[41] French developments have been covered by the contributions of Raucourt,[98,99] and German prewar practices by the monographs of Trappmann[118] and of Peters.[95] Recently, Riemschneider has published a monograph on the new contact insecticides.[100a] Older contributions include those of Cunningham[31] in the 1930's and Bourcart,[20] Wardle and Buckle,[121] Anderson and Roth,[3] and Trappmann[117] in the 1920's. Two books are available on practical insect control, one American[84d] and the other French,[84b] primarily designed for the pest-control operator.

THE CHLORINATED HYDROCARBONS

DDT

p,p'-Dichlorodiphenyltrichloroethane, or, more correctly, 2,2-bis(*p*-chlorophenyl)-1,1,1-trichloroethane, is produced technically as a white amorphous powder, but the pure compound crystallizes in biaxial tabular crystals. The empirical formula is $C_{14}H_9Cl_5$, and chlorine constitutes 50.01% of the molecular weight. Its specific gravity is 1.556 at 25° C. The vapour pressure of DDT has been determined to be equivalent to 1.5×10^{-7} mm Hg at 20° C.[15] This exceptional lack of volatility (for an

organic compound) is responsible for its outstanding properties as a residual insecticide.

DDT is prepared by condensing 1 mole of chloral with 2 moles of chlorobenzene in 98% H_2SO_4 at a temperature of 15° C. The average commercial product contains 70% of the *p,p′* isomer, the remainder consisting mainly of *o,p′*-DDT along with a little DDD, *o,p′*-DDT sulphonate, PDB, and excess chlorobenzene. The purity of the *p,p′*-DDT is increased by using an excess of chloral.

The melting point of purified DDT is 109° C, and its setting point is between 103° and 105° C. Technical DDT shows a melting point of 89° C, and it is considered a satisfactory product if the setting point is not below 88° C. The more highly purified "aerosol grade" of DDT has a melting point of 103° C and is approximately 85% pure.

TABLE 1. Solubility of Certain Chlorinated Hydrocarbons in Organic Solvents

gm/100 cc at 25–30° C

	DDT	Lindane	Aldrin	Dieldrin	Toxaphene
Acetone	58	44	159	54	450
Ethyl alcohol	2	6.4	9.0 *	4.9 *	12
Carbon tetrachloride	45	6.7	...	..	450
Cyclohexanone	116	37	...	..	...
Benzene	78	29	350	75	450
Xylene	53	25	...	..	450

* In methyl alcohol.

DDT is almost completely insoluble in water and is the least water-soluble organic compound known.[60] Its true solubility is 0.0002 part per million of water,[100] although it can form colloidal solutions up to 0.2 ppm in concentration. It is also possible to obtain gravity-stable suspensions of higher concentration, but they are precipitable. DDT is quite freely soluble in apolar organic solvents (see Table 1). Its solubility in aliphatic oils is limited: refined odourless kerosene 4%, crude kerosene 8–10%, no. 2 fuel oil 7–10%. In a natural oil, such as linseed, peanut, or cottonseed oil, the solubility is 10–12 gm/100 cc. Aromatic oils are superior solvents, an American petroleum product such as

APS-202 giving strengths of 45 gm/100 cc at 25° C. When they are refined, superior solvents for DDT are obtained in the form of methylnaphthalenes; an example is *Velsicol AR-50*, in which DDT is soluble to the extent of 55 gm/100 cc. The solubility of DDT in most solvents rises steeply with an increase in temperature.

DDT is very stable at normal temperatures. It decomposes at 195° C, but the decomposition may be inhibited by magnesium oxide, picolinic acid, or salicylalaminoguanidine.[56] It is labile in alkali, which dehydrochlorinates it to the dichloroethylene or the ethane analogue. It is catalytically decomposed in the same way by oxides or chlorides of iron or aluminum. This process may be delayed by solvents such as kerosene, fuel oil, or methylnaphthalenes; propylene oxide also inhibits decomposition of DDT in aerosol bombs. As a consequence of its lability to alkali, DDT is incompatible with kaolin, fuller's earth, and dolomite, and with the alkaloid nicotine. Bentonite, some talcs and pyrophyllites, sulphur, Bordeaux mixture, and the fungicide *Fermate* cause slight decomposition of DDT. Lead and calcium arsenate, Paris green, the fluosilicates, cryolite, hydrated lime, and lime-sulphur are safe as admixtures for this insecticide.

DDT is not normally decomposed by sunlight. It is almost completely stable to ultra-violet light when in solid form, but in oil solution it is slightly decomposed. DDT dusts have been found to lose their toxicity at a faster rate at higher relative humidities,[115] but this may be due to moisture rendering the diluent less compatible. Being water-insoluble, DDT is not leached away by rain. Deposits on citrus foliage in California were found to persist for 40 days before 50% loss, and 90 days before 90% loss, of material occurred.[56a] Tropical temperatures and humidities may decompose DDT comparatively rapidly; hot, dry weather also hastens its loss from orchard foliage, possibly by raising its volatility to an appreciable level.

DDT is formulated in 5% solutions for use as household space sprays, odourless kerosene being the solvent along with a small amount of xylene or methylnaphthalene as co-solvent. It is also put up as 25% emulsion concentrates, where the solvent is methylnaphthalene, cyclohexanone, isophorone, tetralin, or cumene,

the flash point should be above 110° F, which eliminates xylene from consideration.[74] The concentrate contains 15% of an oil-soluble emulsifier such as an alkyl aryl polyether alcohol (e.g. *Triton X-100*), which renders it self-emulsifiable on mixing with water. Emulsion concentrates have been made with a mixture of solvent naphtha or toluene with liquid rosin or turpentine as the solvent, and a soap or a sodium alkyl sulphate (e.g. *Teepol X*) as the emulsifier. The use of casein as an emulsion stabilizer for a concentrate in solvent naphtha allows the material to be shipped as a mayonnaise cream containing 27% water.[73] A fine suspension concentrate (colloidal DDT) may be made by stirring molten DDT into water with a solubilizer, whereupon the insecticide appears as fine crystals. One such concentrate (*Rucide*) contains 40% DDT in 35% water, with 20% petroleum oil and 5% emulsifier.[77]

Since DDT becomes waxy at temperatures approaching its melting point, it resists grinding because of its tendency to cake either during or after the process. It is therefore mixed with an equal amount of pyrophyllite or talc and is ground in a Raymond kiln mill or micronizer mill to a particle size of 0.5–5 microns (μ). When a little wetting agent is added, this product becomes a so-called "wettable powder"; it will go readily into suspension when added to water in the spray tank in concentrations of 1–4 lb/100 gal. If the ground material is further diluted with talc or pyrophyllite, it becomes a DDT dust. Concentrations of 1, 2, 3, or 5% are used for agricultural purposes, and 10% dusts for roach powders. A more effective dust is made by spraying a solution of DDT in a volatile solvent on to the inert diluent in a ribbon blender. These impregnated dusts are so much an improvement that a 3% impregnated dust is as effective as a 5% straight-mix dust,[66] and it kills the insects faster.[32a]

DDT may be effectively included in paints and washes for the treatment of walls to make them residually insecticidal. This stratagem is successful with casein paints, calcimines, and chalk whitewashes. In limewashes the DDT is decomposed by the alkali, but if enough insecticide is added it may retain its toxicity for at least 2 months.[57] A concentration of 3–5% DDT in flat oil paints is very effective.[17] With enamel paints the insecticide is sealed off by the glossy outer film, but these paints may

nevertheless be rendered effective if as much as 20% DDT is added.

Two colorimetric methods are available for the estimation of minute quantities (10 micrograms, i.e. μg) of DDT. One is the Stiff-Castillo method, where a red colour is obtained by heating DDT in pyridine with xanthydrol and KOH; however, the amount of water in the pyridine is critical.[28] The Schechter-Haller method has been generally found to be superior; in this method DDT is converted to its tetranitro derivative, which gives a blue colour with sodium methylate in the case of *p,p'*-DDT and a violet-red colour for *o,p'*-DDT.[104] No colour is given with any other chlorinated hydrocarbons, and the method is the most specific available; it is used for the examination of plant residues, foods, and animal tissues. The Alessandrini modification [*Bull. W.H.O.*, **2**:629 (1950)] is simpler but much less sensitive. DDT may be assessed directly by the spectrophotometer, showing maximum absorption at 236 millimicrons.

DDT may also be estimated by dehydrochlorinating it in alkali and titrating the chloride by Volhard's method. If it is refluxed with metallic sodium and isopropyl alcohol, all the chlorine atoms will be removed from the molecule and the amount of DDT is therefore twice the weight of the chlorine determined (total chlorine method).[41] If it is refluxed with KOH in ethyl alcohol[54] or treated at 45° C with 4.5 *N* ethanolic NH_4OH,[55] only one chlorine atom will be removed (hydrolysable chlorine method). It is possible to modify the conditions so that only the *p,p'*-DDT, and not *o,p'*-DDT or other impurities, is dehydrohalogenated.[61]

Methoxychlor

The methoxy analogue of DDT, namely 2,2-bis(*p*-methoxyphenyl)-1,1,1-trichloroethane, is a white solid which melts at 88° C. It is produced by the condensation of chloral with anisole.[111] The technical material is pale buff in colour and is 88% pure. Like DDT, it is insoluble in water but soluble in many of the common solvents. It may be determined quantitatively, after dehydrohalogenation, by nitration and treatment with sodium methylate according to the Schechter-Haller routine; a pink colour is obtained. The dehydrohalogenated methoxychlor may be

qualitatively detected by the pink colour it gives with 85% N_2SO_4 solution.[8]

DDD

p,p'-Dichlorodiphenyldichloroethane, or tetrachlorodiphenylethane (TDE), is an analogue of DDT which has one less chlorine atom, being 2,2-bis(*p*-chlorophenyl)-1,1-dichloroethane. It is a white crystalline solid with a melting point of 109° C. It is produced by the condensation of dichloroacetal with chlorobenzene.[43] The commercial product has a minimum setting point of 86° C. It exhibits grinding and solubility characteristics similar to those of DDT, and is marketed as a 50% wettable powder (e.g. *Rhothane WP-50*) and a 25% solution in an aromatic oil (e.g. *Rhothane S-215*). It was also developed in Germany under the designation M-1700.[22a]

DFDT, Lucex, and Dilan

The difluoro analogue of DDT, namely 2,2-bis(*p*-fluorophenyl)-1,1,1-trichloroethane, is a solid with a melting point of 45° C. It is appreciably volatile, boiling at 177° C at 9 mm Hg, and thus has less residual persistence than DDT.[91] It was produced commercially in Germany under the name of *Gix*, which is a liquid contaminated by about 10% of the *o,p'* isomer.[22]

2-(*p*-Chlorophenyl)-1,1,2,2-tetrachloroethane has been used as an insecticide in Germany under the name of **Lucex.**[22a] The *p,p'*-dimethyl analogue of DDT, m.p. 90° C, has been used in the United States on a semicommercial scale.[91]

Dilan is the trade name applied to a mixture of 1 part of 2-nitro-1,1-bis(*p*-chlorophenyl)-propane (Compound CS-645A) with 2 parts of 2-nitro-1,1-bis(*p*-chlorophenyl)-butane (Compound CS-674A). These compounds are solids with melting points of 79° and 59° C, respectively, stable to acid and weak alkali, and the mixture has an odour of almonds. The materials are soluble in organic solvents, and an emulsion concentrate is made of 25% *Dilan* in pine oil. They offer about half as much toxic hazard as DDT, and are particularly insecticidal to the Mexican bean beetle.[39a] However, *Dilan* has caused russetting of susceptible varieties of apples.

BHC

Benzene hexachloride, or, more correctly, 1,2,3,4,5,6-hexachlorocyclohexane, has the empirical formula $C_6H_6Cl_6$, from which is derived its original code name of 666; it contains 72.3% of chlorine. As commercially produced, it consists of buff-coloured crystals which have a pronounced musty odour, due to impurities and to breakdown products which subsequently develop. BHC is prepared by the chlorination of benzene in the presence of ultra-violet light; in its absence hexachlorobenzene (C_6Cl_6) is obtained.

Benzene hexachloride, as prepared by this method, consists of a mixture of optical isomers, of which the alpha isomer constitutes some 55–70% of the material (Table 2). In addition, there may be some 4% of heptachlorocyclohexane and 0.6% of octachlorocyclohexane.[97] It is the gamma isomer of hexachlorocyclohexane that is the powerful insecticidal principle, so that the toxicity of BHC is proportional to its gamma content; the usual commercial preparations contain approximately 10–13% of this principle. The gamma isomer may be separated by dissolving BHC in methyl alcohol, which takes up the gamma and delta isomers only; upon evaporation of this methanolic solution the gamma isomer is the first to crystallize out, and it may be purified by solution in and recrystallization from chloroform.[109] Commercial preparations are now available which contain as much as 92% of the gamma isomer (e.g. *Hi-gam*). Purified preparations which contain not less than 99% of the gamma isomer are now given the name of **lindane,*** which replaces the trade name *Gammexane.*

The isomers of BHC are appreciably volatile (Table 2). Although the vapour-pressure values obtained by Slade appear entirely too high, there is a possibility that those obtained by Balson are low. The volatility of BHC in field deposits is sufficient not only to prevent it from showing adequate residual properties, but also to allow it to have a definite fumigant action on insects in crevices. The fumigant effect is an important factor

* After van der Linden, who in 1912 discovered the existence of the isomer.

in laboratory testing of this material. The purified crystals of lindane are colourless, and comparatively odourless when first produced.

TABLE 2. PROPERTIES OF THE ISOMERS OF BENZENE HEXACHLORIDE

	Alpha	Beta	Gamma	Delta	Epsilon
Per cent in BHC	70	5	12	7	3
Melting point, °C	158	312	112.5	138	219
Vapour pressure, mm Hg at 40° C *	0.06	0.17	0.14	0.09	...
Vapour pressure, mm Hg at 20° C *	0.02	0.005	0.03	0.02	...
Vapour pressure, mm Hg at 20° C †	2.5×10^{-5}	2.8×10^{-7}	9.4×10^{-6}	1.7×10^{-5}	

* Values obtained by Slade.
† Values obtained by Balson.

The isomers of BHC are moderately soluble in organic solvents, in the order $\delta > \gamma > \alpha > \beta$. The gamma isomer is 18% soluble in heavy naphtha (b.p. 230–270° C) and 3.2% soluble in paraffin oil (b.p. 138–212° C), when measured as the grams/100 cc taken up at 20° C. It is readily soluble in the methylnaphthalenes and other aromatic oils. Lindane is relatively insoluble in water, the maximum solubility being approximately 10 ppm; of the other isomers, the beta has a solubility of 5 ppm, the remainder 10 ppm.

The isomers of BHC are stable to the effects of light under atmospheric conditions.[26] They are stated to be stable at high temperatures, although when thermally generated as smokes they show the same 30% destruction as DDT. They are stable to the action of hot water and concentrated nitric acid. BHC is not affected by natural chalky or limey waters. But the isomers are susceptible to alkali in the order $\alpha > \delta > \gamma > \epsilon > \beta$,[75] such that all except beta are destroyed by cold KOH, and all are destroyed by boiling KOH.[125] The process is one of dehydrochlorination to 1,2,4-trichlorobenzene, with smaller amounts of 1,2,3- and 1,2,5-trichlorobenzene.[30]

BHC may be quantitatively assessed by the total chlorine method developed for DDT.[126] It may also be determined spectroscopically by means of the absorption band in the ultra-violet

range given by the 1,2,4-trichlorobenzene obtained by alkaline dehydrochlorination of BHC.[81] The gamma-isomer content may be assessed according to the hydrolysable chlorine method by treating the BHC with N alcoholic KOH at 0° C for 50 min (which dehydrochlorinates the alpha, delta, and gamma isomers) and subtracting the value obtained by treating a similar sample for 15 min (which dehydrochlorinates the alpha and delta isomers only).[79] It may also be determined by the separation and crystallization method described above, by cryoscopic methods based on the depression of the freezing point,[21] by chromatographic adsorption,[97] by infra-red spectroscopy,[32] and by bioassay of the insecticidal effectiveness of the sample.[67]

Chlordane

Technical chlordane (U. S. Dept. Agr.), or chlordan (Am. Chem. Soc.), is the name given to a product, formerly called *Compound 1068*, containing not less than 60% of 1,2,4,5,6,7,8,8-octachloro-4,7-methano-3a,4,7,7a-tetrahydroindane, with the remainder (25–40%) being related dicyclopentadiene derivatives. It is a highly viscous liquid, dark amber to brown in colour, with a terpene-like odour. The refined product is pale amber with a faintly aromatic odour. The specific gravity is 1.56 at 60° F, the viscosity 6900 cp at 25° C, and the refractive index 1.56 at 25° C. The empirical formula of the octachloromethanotetrahydroindane is $C_{10}H_6Cl_8$, its molecular weight is 409.8, and its calculated chlorine content is 69.22%. Technical chlordane boils at 175° C at reduced pressure (2 mm Hg). Its volatility is intermediate between that of DDT and BHC, the vapour pressure of the refined product being approximately 1×10^{-5} mm Hg at 25° C.

The octachloromethano-tetrahydroindane (alias -hexahydroindene) occurs as two structural isomers, the *cis* and *trans* forms, which have been named alpha-chlordane and beta-chlordane, respectively. These isomers cannot be separated from each other or from the remaining constituents of technical chlordane by distillation, since the liquid superheats. However, by chromatographic adsorption on aluminum oxide, it has been possible to separate these two isomers and obtain two further derivatives of tetrahydroindene (namely hexachlor and heptachlor); and all

of them are white crystalline solids. In addition a white crystalline solid called trichlor-237 has also been isolated.

The known constituents of technical chlordane are therefore as follows:

a. cis-2,3,4,5,6,7,8,8-octachloro-2,3,3a,4,7,7a-hexahydro-4,7-methanoindene (α-chlordane); melting point 102–104° C.

b. trans-2,3,4,5,6,7,8,8-octachloro-2,3,3a,4,7,7a-hexahydro-4,7-methanoindene (β-chlordane); melting point 104–106° C.

c. 1 or 3a,4,5,6,7,8,8-heptachloro-3a,4,7,7a-tetrahydro-4,7-methanoindene (heptachlor); melting point 92–94° C.

d. 4,5,6,7,8,8-hexachloro-3a,4,7,7a-tetrahydro-4,7-methanoindene (hexachlor or compound 237); melting point 154° C, with decomposition.

e. 1 or 3a,2,3,4,5,6,7,8,8-enneachloro-2,3,3a,4,7,7a-hexahydro-4,7-methanoindene (trichlor 237); melting point 122–123° C.

Of these materials, heptachlor is 4–5 times as insecticidal as technical chlordane, and the *trans*-chlordane is 10 times as toxic as the *cis*-chlordane but not quite as insecticidal as heptachlor.

Technical chlordane is completely miscible with all apolar solvents, including aromatic and aliphatic hydrocarbons, alcohols, ethers, and esters. It is insoluble in water. It should not be heated above 60° C if it is to maintain its toxicity. It is stable to acid and is compatible with dinitro compounds, arsenicals, fluosilicates, other chlorinated hydrocarbons, dithiocarbamates, and sulphur. It is readily detoxified by alkaline dehydrochlorination; thus it is not stored in galvanized iron or steel containers, but in glass, or else aluminum-clad or lacquered steel.

Emulsion concentrates containing 45% or 75% chlordane are made by mixing the technical product with kerosene and adding 10% of a wetting agent. A 90% concentrate may be made by omitting the kerosene. The concentrates are stabilized by the addition of starch or dextrin to retard creaming. Wettable powders are made by spraying chlordane heated to 130° F onto diatomaceous earth in a ribbon blender to give a 50% (wt. wt.) mixture; the wetting agent is then added. Alternatively the 50% mixture may be diluted with pyrophyllite to give 5% or 10% dusts.[23]

Chlordane may be quantitatively determined by the total chlorine methods employed for DDT. It may also be assessed by the hydrolysable chlorine method,[55] two atoms of chlorine being removed per molecule. Liquid technical chlordane gives a purple colour on being heated with diethanolamine and methanolic KOH; and a red colour on being heated with pyridine, ethylene glycol monoethyl ether, and alcoholic KOH. The crystalline constituents of technical chlordane themselves fail to give these colour reactions.[61]

Aldrin and dieldrin

Aldrin (formerly called *Compound 118* or *Octalene*) is 1,2,3,4,10,10-hexachloro-1 : 4,5 : 8-diendomethano-1,4,4a,5,8,8a-hexahydronaphthalene; dieldrin (*Compound 497* or *Octalox*) is the 6,7-epoxy derivative of aldrin. Thus the empirical formulae are $C_{12}H_8Cl_6$ for aldrin, and $C_{12}H_8Cl_6O$ for dieldrin.

Aldrin is a white crystalline solid, with a melting point at 100–103° C. It emits a mild piney odour when warmed. It is much less volatile than lindane and is intermediate between chlordane and DDT in residual effectiveness. It is insoluble in water, but as much as 89 gm/100 cc dissolve in refined kerosene (*Deobase*) at 26–30° C. It is stable to alkali and metallic chlorides. Residues on plants may be determined by the Danish-Lidov colorimetric method. Aldrin is equivalent to lindane in its toxicity to insects.

Dieldrin is an odourless white crystalline solid, with a melting point at 173° C. It is scarcely volatile, showing a residual toxicity whose persistence is comparable to that of DDT. It is less soluble in organic solvents than aldrin (see Table 1), and 4.3 gm/100 cc are taken up by base oil (standard no. 10) at 26–30° C. Although decomposed by strong acid, it is completely stable to weak acids and to alkalis. It is the most toxic and residually effective of the present insecticides.

Toxaphene

Toxaphene (formerly called *Compound 3956*) is a chlorinated camphene whose empirical formula is $C_{10}H_{10}Cl_8$ and which contains 67–69% of chlorine.[129] It is a cream-coloured waxy solid with a mild terpene odour. Toxaphene melts in the range from

65 to 95° C, and its specific gravity is 1.66 at 27° C.[95] It is scarcely volatile, showing only 0.1% loss in weight in being heated to 100° C for 20 hr. It is insoluble in water but highly soluble in organic solvents and oils (Table 1). Lubricating oil will take up 75 gm/100 cc, fuel oil 260 gm/100 cc, and kerosene more than 280 gm/100 cc at 27° C.

Toxaphene is stable either alone or in solution. When heated or exposed to ultra-violet light it is very slowly dehydrochlorinated; at a temperature of 300° C it yields only 10 ppm of HCl per hour. Oil solutions may be stored in clear glass bottles without appreciable deterioration. The dehydrochlorination is hastened by alkali and Fe, but iron containers are safe for storage of toxaphene at room temperatures. There is one labile chlorine atom per molecule, which suggests the use of the hydrolysable chlorine method of assessment. However, toxaphene residues are determined by the total chlorine method, using the nitrobenzene modification of the Volhard titration.[9]

Chlorinated acaricides

Three compounds have been developed for the control of tetranychid mites infesting orchard trees. They resemble DDT in containing two *p*-chlorophenyl groups, but differ in the lack of chlorine in the nucleus of the molecule.

DMC is the name given to di(*p*-chlorophenyl)methylcarbinol (occasionally called DCPC), or, more correctly, 1,1-bis(*p*-chlorophenyl)-ethanol. It is a crystalline solid, of empirical formula $C_{14}H_{12}OCl_2$, with a melting point of 70–71° C. Although susceptible to decomposition by acid, it is stable to alkali and thus compatible with most agricultural chemicals. It is readily soluble in organic solvents (Table 3) and is taken up by D.C. naphtha and Skellysolve B to the extent of 7.2 and 4.3 gm/100 cc, respectively. It is formulated as a 25% miscible concentrate (e.g. *Dimite*). DMC is not easily manufactured and is an expensive material.

DCPM (*Compound K-1875*) is the name given to bis(*p*-chlorophenoxy)methane. It is a crystalline solid of empirical formula $C_{13}H_{10}O_2Cl_2$, with a melting point of 70–72° C.[91] Although hydrolysed by boiling dilute acid, it is stable to alkali.[1] It is

readily soluble in organic solvents (Table 3) but is insoluble in water and (curiously enough) VMP naphtha. DCPM is formulated as a 40% wettable powder (e.g. *Neotran*).

TABLE 3. SOLUBILITY OF CHLORINATED ACARICIDES IN ORGANIC SOLVENTS

	DCPM	DMC	K-6451
Acetone	189	...	130
Carbon tetrachloride	28	...	41
Diethyl ether	87	152	...
Ethyl alcohol	0.5	125	1.4
Benzene	40	110 *	78 †

* Toluene.
† Xylene.

Chlorinated sulphonyl compounds

These materials contain both sulfonyl and *p*-chlorophenyl radicals, and have recently proved valuable as acaricides.

K-6451, or *p*-chlorophenyl *p*-chlorobenzenesulphonate, is a highly persistent mite ovicide, although a poor insecticide. The technical product is a flaky tan-brown material, with a melting point at 80° C. It is insoluble in water but readily soluble in organic solvents (Table 3). The solubilities in cyclohexanone, methylnaphthalene (*Velsicol AR-60*), and kerosene (*Deobase*) are 110, 52, and 2 gm/100 cc respectively. K-6451 is compatible with most of the insecticides. It is formulated as a 50% wettable powder (e.g. the product *C-854*).

Genitol 923 is the 2,4-dichlorophenyl ester of benzenesulphonic acid. It is an effective residual acaricide, but has injured the foliage of orchard trees.

R-242, or *p*-chlorophenyl phenyl sulphone, has proved to be of value as a residual acaricide.

THE ORGANIC PHOSPHATES

HETP

The name of hexaethyl tetraphosphate was given to a commercial product whose composition tallied with the empirical formula $C_{12}H_{30}O_{13}P_4$ and which showed an apparent molecular weight of 506.3. In reality, however, this product is a mixture of linear polyphosphates, linear hexaethyl tetraphosphate, penta-

ethyl triphosphate, tetraethyl pyrophosphate, and triethyl phosphate.[29] The main insecticidal principle is tetraethyl pyrophosphate or TEPP, which is present in proportions between 10 and 20% in commercial HETP.

HETP is a light amber, oily liquid whose freezing point is approximately −40° C, and which on heating decomposes at 145–150° C. Its specific gravity is 1.28–1.29, and its refractive index 1.426 at 27° C. It is produced by reacting 9 moles of ethyl alcohol with 4 moles of phosphorus oxychloride, or more usually by reacting 2–3 moles of triethyl phosphate with 1 mole of phosphorus pentoxide.[58] It was originally marketed in Germany as a 60% emulsion in 20% toluene and 20% emulsifier, under the trade name of *Bladan*.[58a] It is available in North America as the undiluted liquid.

TEPP

If as much as 5 moles of triethyl phosphate are reacted with 1 mole of phosphorus pentoxide, a product is obtained which contains 40% of tetraethyl pyrophosphate and is thus called TEPP.[29] This material is a dark amber to colourless mobile liquid whose freezing point is below −60° C and which decomposes above 165° C. It boils at 150° C at 10 mm Hg, and its specific gravity is 1.19–1.20.

The pure tetraethyl pyrophosphate may be made by treating silver pyrophosphate with ethyl iodide, or may be isolated from commercial TEPP. It is a water-white mobile liquid which boils at 104–110° C at 0.08 mm Hg, and whose refractive index is 1.4200 at 20° C. Its empirical formula is $C_8H_{20}O_7P_2$, its molecular weight 290.2, and its specific gravity 1.1845 at 25° C.[58]

Both TEPP and HETP are readily miscible with water, to the extent that they are hygroscopic. They are miscible with the organic solvents and with aromatic oils; but they are not miscible with kerosene or other paraffin oils, or with petroleum ether. TEPP, like HETP, is marketed as the undiluted liquid (e.g. *Nifos-T*).

Tetraethyl pyrophosphate rapidly hydrolyses in water to produce 2 moles of diethyl phosphoric acid. At a temperature of 25° C, 50% hydrolysis occurs in 7 hr, and at 30° C in 5 hr. Hexaethyl tetraphosphate is hydrolysed in the same way at a

faster rate. As a result of the formation of free phosphoric acid, HETP and TEPP are highly corrosive to metal containers, whether of black iron, galvanized iron, zinc, or tin. Resistant materials include glass, stainless steel, nickel, and lacquered linings; some grades of porcelain are corroded, and reports are contradictory about aluminum. TEPP, like HETP, is marketed in glass bottles or lacquered drums.

TEPP and HETP are incompatible with alkaline materials such as lime, lime-sulphur, and the basic arsenates; their compatibility is doubtful with acid lead arsenate, dinitro compounds, nicotine, pyrethrum, and rotenone; they are definitely compatible with the chlorinated hydrocarbons and elemental sulphur.[7] Since alkaline soaps are incompatible, they are replaced with non-ionic detergents (e.g. *Igepal*) in aphicidal sprays.[56] HETP has been reported to have a highly fumigant effect on insects. A consequence of the rapid hydrolysis of these phosphates is that they have no residual insecticidal action or toxicity hazard.

Preparations of HETP and TEPP may be assessed for their phosphoric acid content by hydrolysis in aqueous NaCl, extraction in benzene, and back-titration to HCl after treatment with NaOH.[7] The concentration of tetraethyl pyrophosphate relative to hexaethyl tetraphosphate may be gauged by the hydrolysis rates, since the former compound hydrolyses much more slowly.[20] Alternatively the tetraethyl pyrophosphate may be separated from related ethyl phosphates by fractionation with chloroform or benzene; it is then hydrolysed to diethyl orthophosphoric acid, which is determined by titration with standard alkali.[59]

Systemic insecticides

Although a number of organic phosphates show systemic properties, the only one that is sufficiently safe for general use is bis(bisdimethylaminophosphonous) anhydride. This compound, also known as OMPA (octamethylpyrophosphoramide) or pyrophosphoryl-tetrakis-dimethylamide or schradan, is available in the United Kingdom as *Pestox III*.* It is prepared by combining 4 moles of dimethylamine with 1 mole of phosphorus oxychloride; the resulting bisdimethylaminochlorophosphine oxide is converted to the sodium salt of the phosphoric acid and com-

* A systemic insecticide marketed in the United States as *Systox* contains 0,0-diethyl-0-2-ethylmercaptoethyl thiophosphate.

bined with more of the phosphine oxide.[29] It is a colourless viscous liquid with a very slight but characteristic odour. Its boiling point is 154° C at 2 mm Hg, and 98° C at 0.002 mm Hg; the specific gravity is 1.24. Like the other organic phosphates, it is miscible with water, organic solvents, and aromatic oils, but immiscible in paraffin oils.[101]

Bis(bisdimethylaminophosphonous) anhydride is not hydrolysed by water or by alkali. It is susceptible to acid hydrolysis, yielding dimethylamine and phosphoric acid. When applied to the roots it is absorbed into the system and translocated to all parts of growing plants; it will spread throughout the tissues of the leaves to which it is applied.[33] Thus it kills all sucking insects, e.g. aphids or coccids, without killing their predators. It is itself a weak contact insecticide and has no residual contact action; its vapour pressure is so low that its fumigant properties are negligible.[16, 85b, 101]

Parathion

This powerful insecticidal compound, formerly known as E-605, is 0,0-diethyl-0-*p*-nitrophenyl thiophosphate, whose empirical formula is $C_{10}H_{14}O_5NPS$. It is made by reacting phosphorus thiotrichloride with sodium ethoxide and treating the product with sodium *p*-nitrophenate. The commercial product (e.g. *Thiophos 3422*) is 95% pure and is a deep brown to yellow liquid, some samples emitting an odour of garlic. The pure compound boils at 375° C and has a refractive index of 1.5360 at 25° C. The vapour pressure of parathion is 0.0006 mm Hg at 24° C; since this allows a vapour concentration of 0.02 mg/litre, it is sufficient to enable it to show a fumigant toxicity.[22a]

Parathion is very slightly soluble in water, to the extent of 20 ppm. It is completely miscible with a variety of alcohols, ethers, and esters, and with aromatic hydrocarbons; it is virtually insoluble in kerosene and other paraffinic oils, and petroleum ether. It is soluble in certain vegetable oils, such as rape oil and olive oil.[22a] Parathion is stable in water, limewater, and acid. In more alkaline reactions, as at *p*H 11, it is rapidly hydrolysed to *p*-nitrophenol and diethyl-*o*-thiophosphoric acid. It is thus incompatible with lime-sulphur, alkaline Bordeaux mixture, and calcium arsenate with lime. It is quite compatible with lead arsenate, the chlorinated hydrocarbons,

elemental sulphur, and the neutral copper fungicides, and with bentonite and diatomaceous earth provided their pH is less than 8.5. Parathion is not affected by oxygen or ultra-violet light, but it must be recorded that when stored in glass bottles it has lost 50% of its activity in 6 months. At temperatures of 130–140° C, parathion commences to isomerize, the thiono sulphur becoming mercapto sulphur.[85]

Parathion is available commercially as 15% or 25% wettable powders, and as 17% emulsifiable concentrates in isopropyl alcohol. Neither the pure material nor the emulsion concentrates are considered to be safe for handling, because of the danger of skin poisoning. The purity of parathion may be assessed by polarography. A colorimetric method of estimation is based upon the reduction of the nitro group of parathion to the amine, followed by diazotization and coupling with naphthylethylenediamine, giving an intense magenta colour; this colour is also given by the oxygen analogue of parathion, namely diethyl-p-nitrophenyl phosphate (also called *para*-oxon).[12]

Methyl-parathion, the dimethyl analogue of parathion, is now the active principle in commercial E-605 in Germany;[85a] in the United States, two-thirds of methyl-parathion have been mixed with one-third of parathion (e.g. *Metacide*). The vapour pressure of methyl-parathion is much greater than that of parathion. Methyl-parathion is 10 times as toxic as parathion to the granary weevil, but is less effective than parathion against the European red mite. Its toxic hazard has been claimed to be less than that of parathion, but there are results indicating that there is little difference in mammalian toxicity between the two compounds.[85a] Para-oxon, or E-600, has been marketed in Germany despite its high toxic hazard. Other promising organic phosphates include Compound 3472 (tetraethyl dithionopyrophosphate) and Compound 838 (the diethoxy thiophosphoric ester of 4-methyl-7-hydroxycoumarin).[45a]

EPN

This is the code name for ethyl p-nitrophenyl thionobenzene phosphonate, an especially effective acaricide and a promising insecticide. It is a dark amber liquid of specific gravity 1.27, and is much less volatile than parathion. EPN is slightly water-

soluble, but dissolves in many organic solvents. This material has been stated to be compatible with lime-sulphur. It is produced as a 27% wettable powder.[25a]

OTHER SYNTHETIC ORGANIC COMPOUNDS

Dinitro compounds

DNOC is the name given to 4,6-dinitro-*o*-cresol, which by older nomenclature was termed 3,5-dinitro-*o*-cresol. It is a yellow crystalline solid, with a melting point of 86° C. It has a slight, sharp odour, and its vapour pressure has been determined as 5.2×10^{-5} mm Hg. It is slightly soluble in water (128 ppm at 15° C) and solutions may be obtained of 2% in kerosene, 20% in aromatic oils, and 40% in xylene. The sodium, potassium, and ammonium salts are freely water-soluble. Monobasic salts of DNOC are completely undissociated at *p*H 7 and completely dissociated at *p*H 2, with a pK of 5.6.[36] DNOC corrodes metal containers unless they are lacquered; the corrosion liberates alkali which reduces DNOC to 4-amino-6-nitrocresol.[17] It is a mordant stain and is a powerful insecticide, ovicide, and acaricide, but its phytotoxicity has restricted its use to the control of grasshoppers and overwintering insects. It is marketed as a dormant spray for orchard application in the form of an aqueous solution containing 40% of sodium dinitro-*o*-cresylate (e.g. *Elgetol*). A similar product is sold as a weedicide concentrate (e.g. *Sinox*). Deposits of DNOC may be directly assessed by extracting the DNOC in ether, converting it to the sodium salt with $NaHCO_3$, and measuring the colour intensity at 440 mμ.[11]

DNCHP is the name given to 2,4-dinitro-6-cyclohexylphenol, a yellow crystalline solid that melts at 106° C and is only slightly soluble in water (15 mg/litre at *p*H 6.5). It is an effective acaricide for tetranychid mites, and it may be applied to the foliage of orchard trees with safety. Its amine salts are freely water-soluble, and a 20% aqueous concentrate of the dicyclohexylamine salt is most commonly employed (e.g. *DN-111*); the ethanolamine and triethanolamine salts are also effective. A 40% solution of DNCHP itself in miscible oil may be used as a dormant insecticide.

DNBP is the name given to 4,6-dinitro-2-*sec*-butylphenol, a crystalline orange solid. A 36% solution of its triethanolamine salt in water is marketed as *DN-289;*[15,63] another commercial formulation is *Elgetol 318.* These materials are effective dormant insecticides for orchard application. **Arathane,** *CR-1639,* or *Karathane* are names given to dinitrocaprylphenyl crotonate, which is an insecticide, acaricide, and mite ovicide. It has been produced as a 25% wettable powder and a 25% emulsion concentrate, and it has a low toxicity to mammals. The weedicide *Sinox General,* dinitro-*o*-*sec*-amylphenol, has proved to give excellent control of tetranychid mites on field crops.[65a]

Organic thiocyanates

These insecticides have been developed for their knockdown properties in fly sprays; most of them are commercially known as **Lethanes.** Lauryl thiocyanate ($C_{12}H_{25}SCN$) is the main constituent of "lorol" thiocyanate, produced by treatment of the alkyl chlorides of the mixed fatty acids from coconut oil with sodium thiocyanate. β-Thiocyanoethyl laurate ($C_{12}H_{23}O_2$-C_2H_4SCN) is the principal constituent of a mixture of similar esters ranging up to the palmitate; a 50% solution of this material in petroleum distillate is marketed under the name of *Lethane 60.* β,β'-Dithiocyanodiethyl ether ($C_4H_8O(SCN)_2$), also called *n*-butylcarbitol thiocyanate, is sold in 90% solution as *Lethane A-70.* It is also produced as a 13.5% dust called *Lethane B-71,* and a 13.5% wettable powder called *Lethane B-72.* β-Butoxy-β'-thiocyano-diethyl ether ($C_8H_{17}O_2SCN$) is put out as a 50% solution, with *Lethane 384* as the commercial name. *Lethane 384 Special* is a mixture of 12.5% β-butoxy-β'-thiocyano-diethyl ether with 37.5% β-thiocyanoethyl laurate in 50% of petroleum distillate.

The insecticide **Thanite** is the result of treating the camphene from pine oil or turpentine with chloroacetic acid and then with an alkyl thiocyanate. The commercial product contains 80% of isobornyl thiocyanoacetate, along with fenchyl and bornyl thiocyanoacetate, and the thiocyanoacetates of secondary terpene alcohols and tertiary terpene alcohols such as terpineol. *Thanite* is a dark aromatic liquid that is applied for direct knockdown of flies and as a synergist for pyrethrins.

Phenothiazine

The compound produced by the cyclization of diphenylamine with sulphur is known as thiodiphenylamine or phenothiazine ($C_{12}H_9NS$). It is a light yellow crystalline solid with a melting point of 185° C; the commercial product is, however, dark green, possibly because of the presence of isomers or polymers. Phenothiazine is insoluble in water; it is slightly soluble in acetone or ethanol but insoluble in chloroform. It is oxidized on exposure to air and sunlight, phenothiazone and or thionol being produced; this process is hastened by lime or bentonite. Phenothiazine has been used as an insecticide for hornfly maggots, the codling moth, and mosquito larvae. It may be quantitatively determined colorimetrically by treating with bromine water and reading at 520 mμ.[44]

Other sulphur compounds

Lauseto-neu, a preparation containing chloromethyl-*p*-chlorophenyl sulphone, was developed in Germany as a powerful louse ovicide. **TMTD,** tetramethyl thiuram disulphide, which is primarily a fungicide, has proved to be an effective stomach insecticide for leaf-feeding beetles. The tetraethyl analogue has been used for control of scabies mites (e.g. *Tetmosol* soap). **IN-4200,** "lorol"-2-thiazolinyl sulphide, has shown promise as an acaricide, but its commercial production has been discontinued. **Aramite** (also called 88-R) is a promising acaricide without phytotoxic properties; its identity is β-chloroethyl-β(*p-tert*-butylphenoxy)-α-methyl ethyl sulphite. **SPC,** or "polychlorocyclane" sulphide, is a derivative of BHC which has been used for the control of locusts in French North Africa and of apple weevil in France (e.g. *Braconyl*).

Miscellaneous organic insecticides and acaricides

Azobenzene ($C_{12}H_{10}N_2$), an orange-red crystalline solid melting at 68° C, has been used as an acaricide in greenhouses as a thermal smoke or a low-vapour-pressure fumigant. **Xanthone** ($C_{13}H_8O_2$), a white crystalline solid melting at 174° C, has been applied as an insecticide and ovicide against the codling moth and orchard mites in the northwestern United States (e.g. the produce *Genicide*). **Flavan,** which is 2′-hydroxy-2,4,4,4′,7-penta-

methyl flavan, has been used as an acaricide; its addition in equal proportions to DDT in orchard sprays is the basis of the preparation termed "mite-killing DDT." **Valone** is the name given to 2-isovaleryl-1,3-indandione, which is an effective lousicide. The name *tert*-butyl valone has been given to 2-pivalyl-1,3-indandione, which has been found to be effective as a lousicide when orally ingested by rabbits. **Pentachlorophenol,** a flaky crystalline solid with a pronounced creosote odour, is marketed as a wood preservative, to give protection from fungous decay and attack by termites or *Lyctus* beetles. **β-Naphthol,** a pleasant-smelling solid with a melting point of 122° C, is the standard material for impregnating tree bands used to control the codling moth. **G-22008,** namely 1-phenyl-3-methylpyrazolyl-(5)-dimethylcarbamate, is an effective insecticide for houseflies and certain aphids. **Dioctyl phthalate,** more correctly di(2-ethylhexyl) phthalate, has been widely tested as an orchard acaricide (e.g. *Compound 899* or *DOP*).

ORGANIC COMPOUNDS OF BOTANICAL ORIGIN

Nicotine

This alkaloid as obtained from natural sources is laevorotatory beta-nicotine and has the shortened name of *l*-β-pyridyl-α-N-methyl-pyrrolidine. The correct nomenclature is *l*-3-(1-methyl-2-pyrrolidyl)-pyridine, or 1-1-methyl-2-(3′-pyridyl)-pyrrolidine. It is a colourless liquid, almost without odour, which boils at 247° C, and whose specific gravity is 1.009 at 20° C. It darkens in light and air, because of an oxidative change, and becomes more viscous and develops a disagreeable odour. Nicotine is an alkaloid with two basic radicals whose dissociation constants (*Kb*) are 1×10^{-6} and 1×10^{-11}; it readily forms salts with any acid, and dibasic salts with many metals and acids.[91] It is appreciably volatile, its vapour pressure at 25° C having been variously determined from 0.0425 to 0.12 mm Hg; at 80° C the vapour pressure is 2.8 mm Hg. Thus nicotine has application as a low-vapour-pressure fumigant in greenhouses; in the field the destruction of aphids is rendered more thorough by its fumigant action, and at the same time there is no residue left to affect beneficial insects or to endanger the consumer.

Nicotine is commercially prepared by its extraction from the coarse parts of the tobacco plant, *Nicotiana tabacum* or *N. rustica*, by treatment with alkali and steam distillation. The yield ranges from 2 to 5% of the dry weight of the plant and may reach as much as 14% in the latter species. The extracted alkaloid consists of 97% nicotine, the other admixed alkaloids including *inter alia* nornicotine, nicoteine, nicotyrine, anatabine, and anabasine.[91]

Nicotine is miscible in water in all proportions at atmospheric temperatures; since this process develops heat in the solution, the miscibility is considered to be due to the formation of a hydrate. At temperatures above 60° C and below 210° C nicotine and water separate out. Nicotine alkaloid is also miscible with alcohol, ether, benzene, and other organic solvents. It is usually marketed as an aqueous solution of the dibasic salt nicotine sulphate, containing 40% of the alkaloid (e.g. *Blackleaf 40*), because this form is more stable and less volatile; incidentally, this salt is dextrorotatory. When it is added to alkaline water or to soap solutions, the free alkaloid is liberated and shows a higher insecticidal activity than the sulphate.

Since alkali has no effect on nicotine preparations beyond heightening their toxicity, nicotine is compatible with all insecticides and fungicides except the definitely acid materials such as DNCHP. It is commonly formulated in 3.6% dusts with alkaline carriers such as hydrated lime, limestone, and other alkaline carbonates, which are termed active carriers because they release the alkaloid. Examples of inert carriers are gypsum and elemental sulphur. Certain acidic dust diluents act as sorptive carriers, such as pyrophyllite, talc, kaolin, and bentonite. Nicotine bentonite (e.g. *Blackleaf 155*) is so stable that the preparation is known as fixed nicotine and is developed, not as a fumigant aphicide, but as a residual stomach poison for caterpillars. Fixed nicotine preparations include nicotine reineckate, silicotungstate, cuprocyanide, tannate, and humate (the last a peat product), which are water-insoluble and effective against the codling moth but not aphids; and nicotine laurate, oleate, linoleate, and naphthenate, which are water-soluble and effective against aphids but not the codling moth. Nicotine is quantitatively assessed by precipitation with silicotungstic acid and

gravimetric determination of the crystalline silicotungstate.[10] Spray deposits may be colorimetrically assessed by measuring the intensity of absorption at 490 mμ after treatment with cyanogen bromide and β-naphthylamine.

Anabasine is β-pyridyl-α-piperidine, or, more correctly, laevo-2-(3′-pyridyl)-piperidine or 3-(2-piperidyl)-pyridine; it is synonymous with neonicotine. It is a colourless viscous liquid, with a boiling point of 281° C and a specific gravity of 1.048. Like nicotine, it is miscible with water and organic solvents, and darkens on standing in air. Its volatility is also similar, the vapour pressure at 79° C being 2.5 mm Hg. Anabasine readily forms salts with acids and metals. It is obtained from the new twigs of *Anabasis aphylla*, a woody shrub whose range extends from Russian Turkestan to North Africa, in which it constitutes 1–2.5% of the dry weight. It occurs in similar amounts in the tree tobacco, *N. glauca*, of the southwestern United States. It may be determined separately from nicotine in that it is precipitable as the fluosilicate from solution in methyl alcohol.

The pyrethrins

The pyrethrin compounds as found in pyrethrum flowers consist of 4 esters, representing the possible combinations of 2 different alcohols with 2 different acids, as follows:

Pyrethrin I: ester of pyrethrolone with chrysanthemum monocarboxylic acid.

Pyrethrin II: ester of pyrethrolone with chrysanthemum dicarboxylic acid-monomethyl ester.

Cinerin I: ester of cinerolone with chrysanthemum monocarboxylic acid.

Cinerin II: ester of cinerolone with chrysanthemum dicarboxylic acid-monomethyl ester.

Pyrethrolone is 2-(2,4-pentadienyl)-4-hydroxy-3-methyl-2-cyclopenten-1-one; this liquid boils at 111° C at 0.1 mm Hg. Cinerolone is the 2-(2-butenyl) analogue of hydroxymethylcyclopentenone, a liquid boiling at 120–124° C at 1–2 mm Hg. Chrysanthemum monocarboxylic acid as it occurs in natural pyrethrins is *d-trans*-2,2-dimethyl-3-isobutenylcyclopropane-1-carboxylic acid and is a liquid boiling at 135° C at 12 mm; the synthetic isomers,

l-trans, *dl-trans*, and *dl-cis*, have melting points of 19° C, 54° C, and 116° C, respectively. Chrysanthemum dicarboxylic acid occurs as the monomethyl ester of the isobutenoic acid analogue, with only one carboxyl group thus free for esterification; it has a boiling point of 140° C at 0.5 mm Hg. Palmitic and linoleic acids also may esterify the pyrethrum alcohols in the natural product.

The pyrethrins and cinerins are obtained from the dried flower heads of *Chrysanthemum cinerariaefolium*, a native of Jugoslavia but now cultivated in Kenya and Japan. The content in most samples ranges between 0.5 and 3.0%, and the main source is the achenes rather than the petals. They may be extracted with alcohol, acetone, or ethylene dichloride, and after evaporation of the solvent they appear as an oleoresin. Esters of the monocarboxylic acid boil at 145° C at 0.05 mm Hg; those of the dicarboxylic acid decompose at this temperature.[116] They are viscous liquids which are insoluble in water but soluble in organic solvents and oils. The pyrethrolone and cinerolone alcohols may be isolated as their semicarbazones.

The pyrethrin esters are hydrolysed in water, and the process is speeded by acids or alkalis. They are therefore incompatible with lime and soaps. They are also oxidized on exposure to air but may be protected by antioxidants such as hydroquinone, pyrocatechol, pyrogallol, isopropylcresol, tannic acid, and 1,4-toluidoanthraquinone. Stored pyrethrum powders lose about 20% of their insecticidal activity in 1 year; it is suggested that the degradation involves a polymerization of the pentadienyl side-chain. Whole flowers are less susceptible than impregnated dusts, and oily concentrates less than aqueous suspensions, to this decomposition.

The ground pyrethrum flowers may be used directly as insect powder, but there is a great waste of the insecticide because of its being locked in the plant cells. The pyrethrins may be extracted in kerosene and then compounded to a content of 3% and sold as concentrates (e.g. *Pyrefume Super 30*). They may be further diluted in odourless kerosene to a 0.1% content and sold as household fly sprays. Aqueous suspensions of pyrethrins may be made from alcohol or acetone extracts of pyrethrum. The pyrethrin esters may be extracted in ethylene dichloride and impregnated onto talc, gypsum, or diatomaceous earth; the

pyrethrum marc left behind after extraction may also be used as the dust diluent. When impregnated onto bentonite, the pyrethrins are held tenaciously.

Synthetic pyrethrins. Esters analogous to the cinerins may now be synthesized. Synthetic cinerolone, isomeric with the natural alcohol, is made by reacting pyruvaldehyde with an alkali salt of 3-oxo-6-octenoic acid at room temperature; the resulting dihydroxyketone is cyclized by treatment with aqueous alkali at room temperature to give the cinerolone isomer.[103] This may be esterified with synthetic chrysanthemum monocarboxylic acid, which is a racemic *cis-trans* mixture, and whose ethyl ester is made by addition of ethyl diazoacetate to dimethylhexadiene.[27] The 2-allyl and 2-isobutenyl analogues of cinerolone may also be made, which give esters that are more stable than natural pyrethrins and are not irritant when used in domestic aerosols. The 2-allyl derivative, known as allethrin, is as toxic as natural pyrethrins to *Musca*, but is inferior in toxicity to *Periplaneta*, *Tribolium*, *Oncopeltus* and a number of field crop insects.[92a] The commercial product is 92% pure.[112a]

Pyrethrin I may be quantitatively determined by its reducing the mercuric sulphate in Denigès reagent to the mercurous ion, which is precipitated as the chloride and titrated with potassium iodate.[10, 11] The chrysanthemum monocarboxylic acid also forms a series of colours, grading from red to blue, with Denigès reagent; this colour reaction is photosensitive.[51] A new method is based on the reaction of hydroxylamine with carboxylic acids, and the formation of coloured complexes with ferric chloride.[81c] Other methods for the pyrethrin esters include the nitromethane-charcoal method,[14] the methoxyl method,[62] and the hydrogenation method.[80] The recent Seil method is based on refluxing with 0.5 *N* ethanolic NaOH, steam-distilling, and titrating with 0.2 *N* NaOH.[106] Allethrins may be determined by the Seil method, the mercury reduction method, or by hydrogenolysis, or by reaction with hydroxylamine.[112a]

Pyrethrin synergists. Certain compounds have the effect of extending the toxicity of pyrethrins, so that very much less pyrethrum is needed in the spray with synergist to achieve the usual knockdown of flies. These compounds are piperonyl compounds with a methylenedioxyphenyl group, or terpene deriva-

tives, or N-substituted amides. Examples of the first group are piperine, a crystalline solid (m.p. 129° C) which is obtained from black pepper; *propyl isome*, a condensation product of isosafrole with *n*-propyl maleate; *sulfoxyl*, the *n*-octyl sulphoxide of isosafrole; sesamin, which is contained to the extent of 0.25% in sesame oil from the *Sesame indicum* plant, *piperonyl cyclonene*, or cyclohexenone, which is a condensation product of alkyl-3,4-methylenedioxystyryl ketone with ethyl acetoacetate; and *piperonyl butoxide*, which is (3,4-methylenedioxy-6-propylbenzyl) (butyl) diethylene glycol ether, a liquid of specific gravity 1.06 and boiling point 180° C at 4 mm Hg.[120] Usually the butoxide is favoured for livestock insecticides, the cyclonene for field-crop insecticides. Sesamin gives a greenish yellow colour with perchloric acid and hydrogen peroxide;[61] piperonyl butoxide gives a blue colour with tannic acid in H_3PO_4 and acetic acid.[72] Pine oil and its products—*Thanite* and terpin diacetate—are synergistic with pyrethrins. *DHS Activator* is the ethylene glycol ether of pinene, a liquid of specific gravity 0.985 and boiling point 257–273° C. Of the N-substituted amides, the one which has been developed as a pyrethrum synergist in louse powders is *IN-930*, or N-isobutylundecylenamide. A compound known as *Van Dyke 264*, the N-(2-ethylhexyl) imide of endomethylene-tetrahydrophthalic acid, is a very effective synergist for allethrin.

Rotenone

The fish poison rotenone is a white solid, crystallizing in the orthorhombic system. Its melting point is 163° C, and its aqueous solutions are laevorotatory. It is almost completely insoluble in water, the solubility being 0.17 ppm at room temperature. Rotenone is soluble in the organic solvents, and particularly the chlorinated hydrocarbons, in the order chloroform > dichloroethane > trichloroethylene > chlorobenzene > benzene, but the solubility is notably low in carbon tetrachloride. It is not readily soluble in petroleum oils; only 0.05% may be dissolved in kerosene, which may be increased to 0.2% with co-solvents. When crystallized from solution in benzene, $CHCl_3$ or CCl_4, the rotenone takes up 1 mole of water of solvation; this does not occur

with other solvents such as acetone, ethanol, or ethylene dichloride.

Rotenone is oxidized on exposure to air, the process being catalysed by light and alkali, yielding the yellow product dehydrorotenone. Oxidation may occur in solutions of rotenone, which turn yellow and then red; but this does not take place in certain solvents such as kerosene, wherein it is quite stable. Rotenone is incompatible with alkaline spray chemicals such as nicotine, hydrated lime, lime-sulphur, and Bordeaux mixture. Alkaline minerals must not be used as dust diluents, clays being incompatible and few grades of talc being compatible.

Rotenone is obtained from the roots of *Derris elliptica* and other congeners which grow in southeast Asia and Indonesia; the dried product called tuba or derris has an average content of 4–5%, ranging up to 13%. It is also obtained from the roots of *Lonchocarpus* spp. native to Central and South America; the dried product is called timbo or cube and contains an average of 8–10% rotenone, with a maximum of 20%. It is also found in various parts of plants belonging to the genera *Tephrosia*, *Millettia*, *Mundulea*, and *Pachyrhizus*. The roots of derris or cube are dried in the sun and ground in hammer mills; the powders are then blended to give a rotenone content between 4 and 5%. The product may be used as a suspension spray at 2 lb/100 gal; it has an average diameter (by surface) of 6 μ. Insecticidal dusts may be made by diluting with inerts to a 1% rotenone content. Alternatively, impregnated dusts may be made by extracting the ground root with chloroform and impregnating the dissolved resin onto pyrophyllite, diatomaceous earth, walnut-shell flour, or pyrethrum marc.

TABLE 4. Occurrence and Toxicity of Derris Insecticides

	Empirical Formula	Melting Point, °C	% Occurrence in Derris Resin	Insecticidal Activity
Rotenone	$C_{22}H_{21}O_6$	163	2–40	100
Toxicarol	$C_{23}H_{22}O_7$	101	8–60	3
Deguelin	$C_{23}H_{22}O_6$	168	12–27	50
Sumatrol	$C_{22}H_{21}O_7$	188	0–15	7
Elliptone	$C_{19}H_{15}O_6$	159	Undetermined	20
Malaccol	$C_{19}H_{15}O_7$	244	Undetermined	Undetermined
Tephrosin	$C_{31}H_{26}O_{10}$	197	Oxidation product	10

In addition to rotenone, derris resins contain a number of related compounds of the fish-poison group[80a] which also are insecticidal, but in less degree (Table 4). All the naturally occurring rotenoids appear to exist as laevo forms. Toxicarol is found as the alpha isomer, and tephrosin appears to be an oxidation product of deguelin.

The rotenone content of a derris preparation may be gravimetrically assessed by crystallization from carbon tetrachloride, which yields the solvate, and recrystallization in pure form from ethyl alcohol. A colorimetric method is available; when the acetone extract is treated with KOH and then acidified with HNO_3 in the presence of sodium nitrite, a red colour is produced.[83]

Veratrine alkaloids

These are a group of alkaloids found in the roots and seeds of liliaceous plants. Probably the most insecticidal are cevadine ($C_{32}H_{49}NO_9$) and protoveratrine ($C_{32}H_{51}NO_{11}$). **Hellebore** root from *Veratrum album* of Eurasian mountain regions contains these two alkaloids, and in addition jervine and pseudojervine and the inactive rubijervine and veratridine. Green hellebore root (*V. viride*) contains cevadine, jervine, pseudojervine, and veratridine. Hellebore is suitable for application to garden fruits shortly before picking, since it detoxifies rapidly. **Sabadilla** seeds from certain species of *Schoenocaulon* which grow in Mexico contain cevadine, veratridine, sabadilline, sabadine, and the inactive cevine. The toxicity of sabadilla seed is considerably increased by a treatment with alkali or heat (150° C). The material is diluted with pyrophyllite or lime to give 10 or 20% dusts; kerosene extracts have also been used. Sabadilla has been favoured for use on forage crops such as alfalfa. It was applied against forest insects in Germany under the name of *Forestit* dust.[84a]

Ryanodine

Ryanodine, the active principle of ryania dust, is an alkaloid whose empirical formula is $C_{25}H_{35}NO_9$ or $C_{26}H_{37}NO_9$, which is neutral and forms no salts. Its absorption spectrum shows a maximum in the ultra-violet at 2685 Å. It is soluble in water and in the organic solvents; although dissolved by diethyl ether,

it is insoluble in petroleum ether.[102] It is stable to light and does not decompose in storage. Ryania dust is obtained from the root and stems of *Ryania speciosa* of Trinidad. It is a stomach and contact insecticide that offers a very effective and safe means of controlling the sugar-cane borer and the corn borer and of protecting domestic gardens against insect attack.[65]

Other botanical principles

The insecticidal product **quassia** contains a group of compounds[50a] which resemble the rotenoids in possessing two methoxy groups, in having similar empirical formulae ($C_{22}H_{30}O_6$ in each case), and in being slow poisons; however, they are water-soluble. They include quassiin (m.p. 205° C) and its isomer neoquassiin (m.p. 225° C), obtained from chips of the wood of *Quassia amara* of Dutch Guiana. A third compound called picrasmin (m.p. 218° C) is found in addition to these two in *Picrasma excelsa* of Jamaica.

The alkaloid **ricinin** ($C_8H_{10}N_2O_2$) is an insecticidal principle found in the castor bean, *Ricinus communis*. The protein ricin, which also occurs in the bean, has no insecticidal power, but it is extremely toxic to higher animals.

Affinin is the name given to N-isobutyl-2,6,8-decatrienoamide, which is as highly insecticidal as the pyrethrins.[1] It is obtained from the roots of *Heliopsis longipes* of Mexico, a plant which had first been misidentified as *Erigeron affinis*. It could also be extracted by petroleum ether from three species of *Heliopsis* native to the southwestern United States.[46a]

Other botanical principles which have been used in China or which have proved very promising in American tests include the following:

Seeds of the croton tree, *Croton tiglium*.
Fruit of the cork tree, *Phellodendron amurense*.
Roots of the thundergod vine, *Tripterygium wilfordii*.
Flowers of *Rhododendron* and *Andromeda* spp. of China.
Seed kernels of the mamey tree, *Mammea americana*.
Extracts of the male fern, *Aspidium filix-mas*.
Bulbs of the cyclamen, *Cyclamen elegans* (miticidal).
Bark of the prickly ash, *Xanthoxylum herculis*.

INORGANIC COMPOUNDS

Lead arsenate

Acid lead arsenate ($PbHAsO_4$) is the particular arsenate of lead that is commonly used on orchard trees and field crops. It has also been termed dibasic lead arsenate, diplumbic or dilead orthoarsenate, diplumbic or lead hydrogen arsenate. It is produced by the addition of arsenic acid (H_3AsO_4) to a suspension of litharge (PbO), whereupon it is precipitated in fine particles. The specific gravity of the pure crystals is 6.05, and that of the amorphous product is 5.9. The commercial product should not contain less than 30% as As_2O_5, and the PbO/As_2O_5 ratio should be less than 2.14. The pure acid lead arsenate is only 0.002% soluble in water.

The precipitate of acid lead arsenate is filtered, dried, and milled down to a particle diameter of 6–10 μ. In this form it readily disperses to form suspensions in water; these are usually made at the strength of 4 lb to 100 gal, and when sprayed onto foliage they give a uniform tenacious deposit. However, additives such as fish oil, soybean oil, casein, or bentonite have been used to enhance spreading and adhesion.[16] The solubility of the commercial product, as measured by dissolved As in distilled water is 0.4%; in hard tap water it may be as much as 4.4% because of the solubilizing action of the dissolved salts (e.g. NaCl). However, deposits of acid lead arsenate are not solubilized by atmospheric CO_2 and dew.

Alkali is a powerful solubilizer of the As in acid lead arsenate. The addition of the hydroxyl ions leads to the production of lead hydroxyarsenate ($Pb_4(PbOH)(AsO_4)_3$), also termed "hydroxy-mimetite," and arsenic acid (H_3AsO_4), which latter is the source of soluble arsenic. It may be temporarily removed by precipitation as calcium arsenate upon the addition of lime, which is for this reason termed a "safener" for lead arsenate. But eventually the calcium arsenate is hydrolysed by the carbonic acid from the atmospheric CO_2 to produce calcium carbonate and the soluble arsenic acid again.

Lead arsenate is frequently applied with lime-sulphur in the same spray. The H_2S associated with the polysulphides is a

solubilizer of lead arsenate by producing lead sulphide and arsenic oxide. Again, excess lime may be added to precipitate the oxide and its acid as calcium arsenate, and this measure in fact has been shown to halve the amount of soluble arsenic in the spray tank. Alternatively, the sulphates of Zn, Mn, or Fe^{++} may be used as correctives since they supposedly precipitate the H_2S as elemental sulphur, which is not a solubilizer. Lead arsenate may be safely mixed with Bordeaux mixture because of the lime in it. It is also compatible with nicotine sulphate, but the soaps often used with this aphicide are powerful solubilizers of arsenic.

For application to trees (e.g. peach) with extremely sensitive foliage, and in maritime areas where rain contains NaCl, **basic lead arsenate** is employed because it is less soluble and less susceptible to being solubilized. It is a lead hydroxyarsenate, probably mainly $Pb_4(PbOH)(AsO_4)_3 \cdot H_2O$, along with some $Pb_5(PbOH)(AsO_4)_4$. It contains less arsenic than the acid salt, the PbO/As_2O_5 ratio being approximately 3.4, and the requirement for As_2O_3 assay being not less than 22%. Basic lead arsenate is converted to acid lead arsenate in acid waters where the reaction is below *p*H 6.5.

Calcium arsenate

Commercial calcium arsenate is a mixture of dicalcium arsenate ($CaHAsO_4$), tricalcium arsenate ($Ca_3(AsO_4)_2$), and pentacalcium arsenate ($Ca_5H_2(AsO_4)_4$). It is produced by adding $Ca(OH)_2$ to arsenic acid to produce the system CaO-As_2O_5-H_2O with an excess of lime. The commercial calcium arsenate is precipitated and dried as a fluffy powder, with average particle diameters as low as 1–2 μ. It has a much higher As_2O_5 content than lead arsenate, ranging between 46 and 64%, and the PbO/As_2O_5 ratio is 3.3–3.4.

The dicalcium arsenate is liable to be hydrolysed by atmospheric carbonation to produce $Ca(OH)_2$ and H_3AsO_4; this process may be inhibited by excess lime. If the commercial product has been made at high temperatures (over 90° C), it contains a large percentage of basic calcium arsenate, $(Ca_3(AsO_4)_2)_3 \cdot Ca(OH)_2$; this is the so-called "safe" calcium arsenate which hydrolyses much more slowly. Calcium arsenate lacks the adhesive proper-

ties of lead arsenate and has been used mainly as dusts for application to field crops and forests. It is incompatible with soaps and fluosilicates, but compatible with nicotine, sulphur, and mineral oils.

Other arsenates

Basic copper arsenate ($Cu_3(AsO_4)_2 \cdot Cu(OH)_2$ or $Cu(CuOH)AsO_4$), a copper hydroarsenate, is a superior arsenical that has been developed comparatively recently. It is as insecticidal as lead arsenate but has the advantage of being quite insoluble and resistant to hydrolysis by water, carbonic acid, or lime. Analysis of commercial preparations yields 41% arsenic oxide and 56% copper oxide.

Magnesium arsenate, which is a mixture of salts analogous to the calcium arsenate series, has been used for control of Mexican bean beetle where lead or calcium arsenate proved inadequate. Ferric arsenate and aluminum arsenate have given promising results. Ferrous, manganous, zinc, and barium arsenates proved to be inferior to lead arsenate.

Arsenites

The salts of arsenious acid are derived from **arsenious oxide** (As_2O_3), called white arsenic. This oxide is a by-product of the roasting of mineral ores, which sublimes at 120–150° C and then collects by condensation in the flues; it is the raw material from which all the arsenicals are manufactured. Arsenious oxide is soluble in alkaline water and has been used in insect baits. By dissolving it in aqueous NaOH, **sodium arsenite** may be prepared; this consists of a mixture of the orthoarsenite (Na_3AsO_3) and the metarsenite ($NaAsO_2$). This material, which contains 82% As_2O_3, has been widely used in grasshopper baits. By dissolving white arsenic in excess of lime, **calcium arsenite** is produced; it has been used as dusts against locusts and has also been applied to crops. A mixture of calcium arsenite and calcium arsenate, a by-product of dye wastes, was once marketed and used under the name of *London purple*. Zinc arsenite has also been used on crops but is somewhat phytotoxic.

The **copper arsenites,** $Cu(AsO_2)_2 \cdot H_2O$ or copper metarsenite, and $Cu_3(AsO_3)_2 \cdot 3H_2O$ or tribasic copper orthoarsenite, which

are grayish green crystals, have been safely applied to foliage. A complex of copper metarsenite and copper acetate, of the probable composition $(CH_3 \cdot COO)_2Cu \cdot 3Cu(AsO_2)_2$, has been widely used under the name of **Paris green** for the control of potato beetles, cotton pests, and Anopheline larvae. It was also known as *Mitis green* or *Schweinfürtergrün*, and contained 57% As_2O_3.

The percentage of arsenic in the usual arsenical insecticides may be assessed by treatment with cuprous chloride, distillation of the arsenious chloride, and titration with iodine.[10] The determination of arsenic in residues is accomplished on a micro scale by the Gutzeit method or bromate method.[11] The uptake of both arsenic and lead may be readily determined by the radioactive tracer method.[92b]

Fluorine compounds

Sodium fluoride (NaF) has been used in insect baits and traps. It is commonly employed in roach and ant powders; usually blended with pyrethrum, borax, and inert diluents, it is ground to a particle size of 5–10 μ. It is too soluble in water (4% at 15° C) to be used safely on plants. However, barium fluoride is relatively insoluble and is highly insecticidal.

Sodium fluosilicate, more correctly sodium fluorosilicate or silicofluoride, has the empirical formula Na_2SiF_6 or $2NaF \cdot SiF_4$. It is made by combining sodium carbonate with the product of hydrofluoric acid and silica. It appears as a white powder of 25 μ average particle size, which has a true specific gravity of 2.755 and a high bulk density of 30 cu in./lb; this is often remedied by adding 30% of powdered alumina. Sodium fluosilicate is used in roach powders, grasshopper baits, and mothproofing fluids. It may show phytotoxicity because it is slightly water-soluble (0.65% at 17° C) and forms soluble NaF with salty water; lime is a safener only if used in large amounts.

Barium fluosilicate, $BaSiF_6$, is relatively insoluble in water (0.03% at 21° C) and is therefore safe to use on foliage. But it is more expensive than cryolite and is incompatible with alkaline spray materials such as Bordeaux mixture, lime-sulphur, nicotine, and soap. Of the other fluosilicates, the K salt is too expensive, the Ca salt hydrolyses to the free acid in water, the

Mg salt is not as suitable as barium fluosilicate, and the remainder are not sufficiently insecticidal.

Cryolite, which is sodium fluoaluminate or sodium aluminum fluoride, has the empirical formula Na_3AlF_6 or $AlF_3 \cdot 3NaF$. Natural cryolite may be obtained from deposits in Greenland, and the material is crystalline and 98% pure, with silica, iron oxide, and sodium sulphate as impurities. Synthetic cryolite is amorphous, and it is made by combining aluminum fluoride, ammonium fluoride, and sodium chloride. The solubility in water of cryolite has been variously reported as 0.004%[34] and 0.06%.[44] The *p*H of the suspensions has been reported to be approximately 6.2,[44] but it has been found that the imported cryolite ranges from 3.6 to 6.1 and the American product from 7.5 to 8.1 in *p*H.[34] Cryolite may be safely used with soaps or oils, but it is decomposed by lime to form calcium fluoride.

Fluorine compounds may be quantitatively assessed by ashing and conversion to lead chlorofluoride. The amount of Ag required to combine with the Cl in the PbClF is measured by titration of the remaining $AgNO_3$ with potassium thiocyanate.[44]

Miscellaneous inorganic insecticides

Tartar emetic, or potassium antimonyl tartrate ($K(SbO)$-$C_4H_4O_6 \cdot \frac{1}{2}H_2O$), is prepared as a white powder by heating antimony oxide in a solution of acid potassium tartrate. It has a solubility of 5.3% in water, and is used in sweetened bait sprays for the control of fruit flies and thrips. Recently the cheaper antimony calcium tartrate has been found to be just as effective. Tartar emetic may also be used in ant poisons. **Borax** ($Na_2B_4O_7$) and boric acid (H_3BO_3) have been used for the control of maggots and in ant traps and cockroach powders. The latter compound has been included in anti-blowfly dressings for sheep. **Thallium** has also been used in ant baits as thallous sulphate ($TlSO_4$) or thallium acetate. **Zinc phosphide,** primarily a rodenticide, has been effectively used in field baits for mole-crickets.

Barium has formed the base of cheap insecticidal dusts for use on plants. Barium chloride has been used in Russia, and barium carbonate has been employed as a slow-acting insecticide for the Mexican bean beetle. **Copper,** a constituent of

many fungicides and of Paris green, has been tested in the form of cuprous cyanide and cuprous thiocyanate, but these compounds proved to be no better than the arsenicals.

Mercury is also toxic to insects, and mercurated organic compounds have been developed as fungicides to accompany lead arsenate sprays in Europe.[9a] Calomel (mercurous chloride, $HgCl$) and corrosive sublimate (mercuric chloride, $HgCl_2$) are widely used as water-soluble insecticides against the cabbage maggot and onion maggot. The vapour of elemental mercury is used domestically in India to prevent infestation of stored products by insects. **Selenium** is employed as a systemic insecticide and acaricide. It is usually applied to the soil as sodium selenate (Na_2SeO_4) at rates between 1 and 10 ppm. Organic preparations of selenium are available in proportions equivalent to $(KNH_4S)_5Se$ (e.g. *Selocide*).

Sulphur and lime-sulphur

Elemental sulphur (in the rhombic form) is a yellow solid melting at 113° C and with a specific gravity of 2.07; it is insoluble in water. It originally appeared as an acaricide in the form of "flowers of sulphur," crystals recondensed after sublimation. This material is nowadays more finely ground, the extreme being "micronized sulphur," produced in an air-grinding apparatus. More finely divided particles are obtained in "colloidal sulphur," precipitated from several dissolved sulphur compounds in various ways. Another source is "flotation sulphur," produced by oxidation of the H_2S recovered in aqueous alkali from coal-gas fumes.

Calcium polysulphides have been concluded to be the active constituent of **lime-sulphur** mixtures, which are applied to orchard trees to serve as a fungicide, acaricide, and scale insecticide. Although they have never been isolated in pure form, their existence is deduced from the proportion of S to Ca in the clear solution, which has been found to have an average molecular ratio of 4.68. It is concluded that they exist as mixtures of a series of polysulphides ranging from calcium pentasulphide (CaS_5) and higher, down to calcium monosulphide (CaS). The polysulphides react as if they were combinations of calcium monosulphide with additional sulphur, since the monosulphide

sulphur of the polysulphides may be titrated separately. There is good evidence that the biological activity of polysulphides increases along with the proportion of sulphur in them.

These compounds are prepared as a lime-sulphur mixture by heating an aqueous suspension of lime ($Ca(OH)_2$) with elemental sulphur (S). Two parts by weight of sulphur are used for every 1 part of stone lime or every $1\frac{1}{3}$ part of hydrated lime, and the total amount of the two solids added to the water ranges from 28 to 60% by weight. The reaction products go into a true solution, whose colour changes from light yellow to deep orange-red. The constituents of these solutions, as determined after evaporation, consist of 65% calcium polysulphides, 8% calcium thiosulphate (CaS_2O_3) and 10% elemental sulphur. But preparations may be obtained where as much as 94% of the sulphur is in the form of polysulphides.

The strength of the preparation, i.e. the concentration of biologically active sulphur compounds, is indicated by the specific gravity of the solution. The standard strength for commercial lime-sulphur solutions has been set at 32° Baumé at 60° F, equivalent to a specific gravity of 1.283, and corresponding to a sulphur content of 25% or 2.6 lb of commercial sulphur per U. S. gallon. This should ensure that the strength of calcium polysulphides in the solution is not less than 29%. The polysulphide content of the lime-sulphur solution may be expected to be proportional to its specific gravity, provided no adulteration has occurred. The total sulphur may be determined by precipitation as $BaSO_4$, the sulphide sulphur by precipitation with ammoniated $ZnCl_2$, and the monosulphide equivalent by direct titration with iodine.[44]

FUMIGANTS

A great number of volatile organic compounds are sufficiently toxic to be effective as insect fumigants. And indeed a considerable variety of compounds has been developed commercially. The first limiting factor is inflammability; ethylene oxide, the simple esters, carbon disulphide, and ethylene dichloride require dilution with CO_2 or CCl_4 for safety. The second limiting factor is the toxic hazard to the operator, but this consideration has not

prevented HCN from being widely used. It is a disadvantage for the fumigant to be highly adsorptive or highly water- and fat-soluble or absorptive; e.g. CS_2, HCN. It is advantageous for the gas to be readily desorbed and to leave no residue, as is the case with methyl bromide, ethylene oxide, and chloropicrin; these vapours are all highly penetrating. It is of course an advantage for the fumigant to be highly insecticidal, although a compound that is as weakly toxic (to insects) as carbon tetrachloride may have its place because of other desirable characteristics. The combination of high volatility with high toxicity is an advantage (e.g. HCN, methyl bromide, chloropicrin) for the short-term fumigation of closed spaces; but scarcely volatile materials such as naphthalene, PDB, and nicotine have been used successfully, and low-vapour-pressure materials are preferred as spot fumigants and soil fumigants (e.g. ethylene dibromide, hexachloropropene). One of the main considerations in a choice of fumigants is the cost of the materials and their application.

TABLE 5*a*. PROPERTIES OF INSECT FUMIGANTS

Compound	Boiling Point, °C	Specific Gravity of Liquid	Specific Gravity of Gas	Lower Limit of Inflammability, %[71]	Formula
Sulphur dioxide	−10	1.50	2.3	Non-inflamm.	SO_2
Methyl bromide	5	1.732	3.2	13.5	CH_3Br
Ethylene oxide	11	0.887	1.5	3.0	$(CH_2)_2O$
Hydrogen cyanide	26	0.697	0.94	5.6	HCN
Methyl formate	32	0.973	....	5.0	$HCOOCH_3$
Carbon disulphide	46	1.263	2.63	1.2	CS_2
Ethyl formate	54	0.922	....	Inflamm.	$HCOOC_2H_5$
Methallyl chloride	72	0.925	....	Slightly inflamm.	$CH{=}C(CH_3){-}CH_2Cl$
Carbon tetrachloride	76	1.595	1.65	Non-inflamm.	CCl_4
Acrylonitrile	77	0.801	....	Inflamm.	$CH_2{=}CH{-}CN$
Ethylene dichloride	84	1.257	3.5	6.2	$CH_2Cl{\cdot}CH_2Cl$
Trichloroacetonitrile	85	1.440	4.95	Non-inflamm.	$CCl_3{-}CN$
Chloropicrin	112	1.692	....	Non-inflamm.	CCl_3NO_2
Ethide	124	1.415	....	f.p. 136° C	$CH_3{-}CCl_2NO_2$
Tetrachloroethane	146	1.600	5.8	....	$CHCl_2{-}CHCl_2$
Dichloroethyl ether	178	1.220	5.5	f.p. 85° C	$(CH_2Cl{-}CH_2)_2O$

Methyl bromide (Table 5*a*) is the most generally useful of insect fumigants at the time of writing. It has a slight sweetish odour and is non-inflammable, although mixtures of 14% by volume in air may be exploded by a spark. It is slightly soluble in water and considerably soluble in fat solvents; it is not ad-

sorbed on fruits to any extent but it is absorbed into nuts and fatty foods and can form a chemical combination with proteins. Since it is a highly penetrating gas and also can be rapidly desorbed, methyl bromide is particularly useful for low-temperature fumigation. It is widely used for fumigation of dormant nursery stock at 2 lb/1000 ft^3, of greenhouses at 1 lb/1000 ft^3, and of soil at 4.7 cc/ft^2. It is a favoured fumigant for mills, warehouses, ships, and freight cars, where it is used at the rate of 1–3 lb/1000 ft^3. The gas is released from canisters or cylinders in which it is kept liquid under its own vapour pressure.

TABLE 6. Volatility and Insecticidal Activity of Fumigants

	Boiling Point, °C	Vapour Pressure, mm Hg at 25° C	Vapour Saturation,* mg/litre at 25° C	LD_{50} for Tribolium, mg/litre at 25° C
Sulphur dioxide	−10	>760	2670	6
Methyl bromide	5	1824	2860	11
Ethylene oxide	11	>760	1800	18
Hydrogen cyanide	26	739	1140	0.6
Carbon disulphide	46	361	1470	61
Carbon tetrachloride	76	114	940	185
Ethylene dichloride	84	80	430	38
Trichloroethylene	87	73	512	108
Chloropicrin	112	24	212	5
Dichloroethyl ether	175	1.1	23	1.6
Hexachloropropene	203	0.3	6.6	1.1
Heptachloropropane	240	0.09	1.4	2.5

* At temperatures above b.p. $= \dfrac{\text{m.w.} \times 1000}{22.4} \times \dfrac{273}{298}$ mg/litre

At temperatures below b.p. $= \dfrac{\text{m.w.} \times \text{v.p.}}{18.6}$ mg/litre

Ethylene oxide is a relatively odourless gas with good penetrating properties, and it is therefore particularly useful at low temperatures; moreover it is non-corrosive and leaves no residue. Ethylene oxide is used in mills and warehouses at a dosage of 2 lb/1000 ft^3. Since it is inflammable, it is mixed with 9 times its volume of CO_2 (e.g. *Carboxide*) which aids its toxicity by keeping the insects' spiracles open. **Sulphur dioxide** (Table 6), a gas with a suffocating odour, is used as a fumigant primarily

for preventing the development of moulds on dried fruits and for rodent extermination. But it is also effective against insects at a concentration of 5 lb 1000 ft^3, the vapour being produced by burning sulphur or emission from 150-lb cylinders. Sulphur dioxide is 10% water-soluble, and the resulting sulphurous acid is highly corrosive.

Hydrogen cyanide has been widely employed as a fumigant for buildings, and even for citrus trees. Although it has a penetrating odour of bitter almonds, it is toxic in such low concentrations that its use requires the admixture of 5% chloropicrin or cyanogen chloride as a warning gas. It is inflammable only at very high vapour concentrations (Table *5a*). HCN is highly adsorptive, which makes it effective at lower temperatures, but it also becomes difficult to remove by desorption. In addition, it is readily soluble in water, and hence is highly absorptive. It may be generated by atmospheric humidity from calcium cyanide and calcium acid cyanide; the commercial powders yield 55% of their weight as HCN. It also may be released from cellulosic discoids on which it has been held by adsorption (e.g. *Zyklon*). The traditional method is to drop NaCN into dilute H_2SO_4; this may be weighed into paper or zinc-foil bags, or compressed into eggs, 1 lb being dropped into 5 lb of 50% H_2SO_4. Higher concentrations of H_2SO_4 are liable to hydrolyse the HCN into CO and NH_3. **Methyl formate** is highly inflammable and must be diluted with 2.3 parts of CO_2; ethyl formate requires dilution with 6 parts of carbon dioxide.

Carbon disulphide is a cheap fumigant handicapped by an unpleasant smell of H_2S. Since it is extremely inflammable and explosive, it is diluted with 4 parts of carbon tetrachloride. Although insoluble in water, it is highly soluble in fatty materials. Carbon disulphide is highly adsorptive and penetrating and is liable to leave yellow stains. It has proved useful as a soil fumigant and has been employed to fumigate warehouses, dwellings, and stored grain. **Methallyl chloride**, i.e. β-methylallyl chloride, is a European soil fumigant; it is inflammable when in high vapour concentrations. **Methanesulphonyl fluoride**, $CH_3{-}SO_2F$, proved to be a highly effective greenhouse fumigant in Germany, but its hazards to man are too serious.[illegible]

Carbon tetrachloride is not inflammable, which makes it valuable as a fumigant for dwellings despite a low insecticidal toxicity. It is often used as a diluent for ethylene dichloride or ethyl acetate. When CCl_4 is employed alone for grain fumigation, a dosage of 30 lb/1000 ft^3 is required. **Acrylonitrile** is a useful low-vapour-pressure fumigant for dead spots in flour mills and for bedbug control. Being inflammable, it may be mixed with an equal amount of CCl_4, and the mixture proves to be a more effective insecticide than acrylonitrile alone. **Trichloroacetonitrile** has been used as a louse fumigant in Germany and for treatment of stored products in Italy. It is not inflammable but is highly lachrymatory. **Ethylene dichloride**, or 1,2-dichloroethane, has a pleasant chloroform-like odour but is nevertheless a self-warning gas. Since it is inflammable, 3 parts of ethylene dichloride are diluted with 1 part of CCl_4. It is non-corrosive and is used as a mill or domestic fumigant at 6 lb/1000 ft^3 and may be applied by spraying. It can also be used as a soil fumigant in 15% emulsion.

TABLE 5*b*. PROPERTIES OF INSECT FUMIGANTS (*cont'd*)

Compound	Boiling Point, °C	Specific Gravity of Liquid	Melting Point, °C	Formula
Trichloroethylene	87	1.456		$CHCl{=}CCl_2$
Propylene dichloride	97	1.159		$CH_3{-}CHCl{-}CH_2Cl$
Dichloropropene	108	1.218		$CH_2Cl{-}CH{=}CHCl$
Ethylene dibromide	131	2.182	10	$CH_2Br \cdot CH_2Br$
p-Dichlorobenzene	173		56	$C_6H_4Cl_2$
o-Dichlorobenzene	182	1.298	−18	$C_6H_4Cl_2$
Hexachloropropene	203	1.75	<0	$CCl_3{-}CCl{=}CCl_2$
Naphthalene	218	.....	80	$C_{10}H_8$
s-Heptachloropropane	240	1.8	11	$CCl_3{-}CHCl{-}CCl_3$

Trichloroethylene (Table 5*b*) constitutes a slightly more insecticidal, non-inflammable substitute for carbon tetrachloride. **Propylene dichloride**, or 1,2-dichloropropane, is used in 15% emulsions as a soil fumigant. A successful commercial soil fumigant consists of 50% 1,3-dichloropropene, 25% propylene dichloride, and 25% of trichloro and tetrachloro derivatives (e.g. *D-D Mixture*). **Ethylene dibromide** is also used as a soil fumigant as a 10 or 42% solution in naphtha, and can effectively control

wireworms at a dosage of 40 lb of the compound per acre. It is also a highly effective spot fumigant in mills. **Tetrachloroethane** has seen occasional use as a greenhouse and soil fumigant. **Hexachloroethane** has been applied for corn earworm control and quite frequently has been used as an admixture or substitute for PDB for treatment against clothes moths. **Chloropicrin** is a highly insecticidal, self-warning, sweet-smelling lachrymatory gas that has little fire hazard and is highly penetrating. Since it is not water-soluble it is not absorbed by foods, and it is not reactive with metals and drapes. It is used for fumigation of mills, warehouses, and grain at a concentration of 2 lb/1000 ft^3; its effectiveness may be enhanced by admixture of CO_2. **Ethide**, or 1,1-dichloro-1-nitroethane, is also highly insecticidal and is used at a dosage of 1.5 lb/1000 ft^3.

Dichloroethyl ether, the β,β' isomer, is a liquid with a pungent irritating vapour that has proved effective as a soil fumigant against the peach borer. **ODB**, *o*-dichlorobenzene, is a liquid that acts as a soil fumigant for termites and leatherjackets (*Tipula* larvae). **PDB**, *p*-dichlorobenzene, is useful as a soil fumigant and is very widely employed in the form of moth balls to fumigate clothes in the home. **Naphthalene** has also been employed for the same purposes. The literature on soil insecticides has recently been summarized in a special publication.[59] **Hexachloropropene** and heptachloropropane (both symm. and asymm. isomers) are exceptionally persistent insecticides suitable for the protection of dead spots in flour mills.

OILS, SOLVENTS, AND DETERGENTS

Mineral oils

These liquids are composed of a mixture of hydrocarbon oils, which may fall into any one of four classes: paraffins, straight-chain saturated compounds of empirical formula C_nH_{2n+2}; olefins, unsaturated straight-chain compounds with at least one C=C double bond; aromatic compounds, unsaturated cyclic compounds containing benzene and similar rings; and naphthenes, saturated cyclic compounds containing cyclohexane or cyclopentane rings. As obtained from natural strata, oils differ in their

content of these hydrocarbons; for example, Pennsylvania oils are rich in saturated paraffins and are classed as paraffinic; Mexican Gulf and Californian oils contain a large proportion of aromatic and naphthenic compounds and are classed as asphaltic.

Within these classes, oils may be classified according to their molecular weight. This may be assessed by measurements of their boiling range and their viscosity. The viscosity is measured in the Saybolt universal viscosimeter by the time in seconds that is required for 60 cc to flow through an orifice at 100° F; it is expressed as seconds Saybolt, or SSU. British determinations are in Redwood units, and European work is based on the Engler viscosimeter. It is therefore best to express it as the absolute viscosity in poises or centipoises at 25° C or other specified temperature. Another criterion of oils is their specific gravity, which may be measured and expressed as degrees Baumé or degrees A.P.I. (American Petroleum Institute). The refractive index is useful and is determined with the Abbe-type refractometer. The aniline point, involving the temperature relation of the reaction of the oil with dry aniline, is helpful in classification. The flash point also should be determined by the open-cup or closed-cup method. For spraying work, it is usually agreed that the flash point should not be below 125° F, which eliminates the gasolines, naphthas, benzene, and xylene as being too inflammable.

Oils are fractionated from crude petroleum oil by their distillation and recondensation at different levels in distillation columns. At present the liquid fractions in order of their volatility, apart from the volatile natural gas, are gasoline, kerosene, gas oils, and lube oils; the solid residue is petrolatum or paraffin wax (from paraffin crudes) and petroleum pitch or asphalt (from asphaltic crudes). The cyclized hydrocarbons may be separated as naphthas. The unsaturated hydrocarbons may be separated from the saturated hydrocarbons by refinement. The contents of unsaturated hydrocarbons in an oil may be assessed by sulphonation of the oil with 4 times its volume of 38 N H_2SO_4 at 60° C. The purity of the oil, as far as saturated hydrocarbons are concerned, may be gauged by the proportion of unsulphonated residue and expressed as per cent U.R. (A.S.T.M. Designation: D483-40).

Kerosenes are employed as solvents for pyrethrins in fly sprays, and for DDT and other chlorinated hydrocarbons in sprays applied from aircraft for biting-fly control. The lighter kerosenes have a boiling range of 360–480° F, and the heavier of 425–510° F. Their viscosity is too low to be measured accurately on the Saybolt viscosimeter, but it is of the order of 1–2 centipoises at 25° C and may be measured on a special Saybolt thermoviscosimeter. It is believed that kerosenes are composed of hydrocarbons having from 10 to 16 carbon atoms per molecule. The kerosenes may be sulphonated to give odourless kerosene and other refined grades (e.g. *Deobase*), or they may be deodorized by the addition of deodorants such as *Neutroleum alpha.*

Fuel oils resemble the heavier kerosenes in their boiling and viscosity characteristics, which vary widely. They are used as solvents for DDT in biting-fly control. The distillate fuel oil recommended for mosquito larviciding in the absence of DDT had the following characteristics: viscosity, 35–40 SSU; gravity, 35–40 A.P.I.; and 50% distillation at 510–550° F.

Gas oils have a boiling range of 480–570° F and contain 15–18 carbon atoms per molecule. The lighter components of this fraction constitute stove oil (b.p. 330–570° F), and the heavier fraction becomes diesel oil (b.p. 400–700° F). These unrefined classes contain too many toxic sulphonatable materials to be safe for use on plants. But mineral seal oil, a heavy summer oil, may be made by refinement of diesel oil.

Summer oils are higher fractions than kerosene that are applied in aqueous emulsion to the foliage of orchard and shade trees for the control of mites and scale insects. The light summer oils are highly refined, containing at least 92% of unsulphonated residue. Their boiling point is such that 52–79% of their weight has distilled at 636° F, and their viscosity is 40–65 SSU. The number of carbon atoms per molecule ranges from 14 to 18. Medium summer oils are similarly refined, with 28–49% of their weight distilling at 636° F, and a viscosity of 65–85 SSU. Heavy summer oils have a viscosity in excess of 85 SSU, and only 10–25% distils at 636° F; they require a further refinement to not less than 94% U.R. Less highly refined heavy oils may be used as dormant oils, although the "Superior"

type of dormant oil developed at Geneva, N. Y., has as much as 90% U.R., and is mainly paraffinic.

Lubricating oils are not employed as solvents for agricultural insecticides, but in many cases they have been used successfully for dormant emulsion sprays. They extend over a wide range of viscosity, the lightest being SAE 10 (for winter automobile lubrication) and the heaviest SAE 70 (for motorcycle lubrication). The lighter lube oils have a viscosity of 70–110 SSU, and the heavier grades extend up to 330–360 SSU.

Medicinal paraffin includes oils of 150–250 SSU viscosity which are used as laxatives (e.g. *Nujol*). They are very highly refined (100% U.R.) and have been employed as insecticides for the corn earworm.

Naphthenes are volatile oils that are too inflammable for use as insecticide solvents. But the highest fractions have a flash point of 140° F, which makes them safe for the treatment of upholstery where a rapidly evaporating solvent is required. Their boiling point ranges from 370 to 412° F (e.g. Stoddard's solvents).

TABLE 7. CHARACTERISTICS OF *Velsicol* METHYLATED NAPHTHALENE SOLVENTS

	AR-50	AR-50G	AR-55	AR-60	NR-70
Specific gravity at 60° F	0.960	0.943	0.922	0.993	0.983
Viscosity, SSU at 100° F	35	35	35	40	35
Minimum initial boiling point, °F	420	415	415	460	420
Maximum final boiling point, °F	520	530	550	570	680
Flash point (open cup), °F	200	200	200	220	200
Solvent power for DDT, % at 15° F	35	30	25	35	30

Methylnaphthalenes are components of asphaltic petroleum oils as well as of the coal-tar oils. They are themselves insecticidal and have proved themselves particularly valuable as initial solvents for DDT (e.g. *Arosol 151B*). Highly refined fractions are now available (e.g. the *Velsicols*), which may also be used to stabilize the droplets in liquefied gas aerosols. Their properties are shown in Table 7. All the *Velsicol* solvents have an aromatic odour, but all are almost colourless with the exception of NR-70.

Miscible oils. These are proprietary products consisting of a solution of emulsifier in gas oil or lube oil. Cresylic or carbolic acid soaps, resinates, sulphonated fatty acids, and petroleum β-sulphonates have been employed as emulsifiers. The unsaturated oils removed by sulphonation may be oxidized at the double bonds and made available commercially as the sodium salt of the sulphonic acids (e.g. *Penetrol*) for use as emulsifiers and spreaders. Miscible oils usually contain a small amount of water and a mutual solvent such as cresylic acid to ensure that they readily emulsify on dilution and mild agitation.

Tar distillate

This material is the condensed distillate from the destructive distillation of coal to produce illuminating gas and coke. It consists of a mixture of aromatic compounds (benzene, naphthalene, anthracene, and other ring compounds with their methyl derivatives), tar bases (pyridine, quinolines, etc.), and tar acids (phenol, cresols, etc.). It has been widely used for dormant sprays in Europe under the name of *Carbolineum*. Satisfactory tar distillates start to boil at 410° F (210° C) and not more than 65% of their volume has boiled at 671° F (355° C). Specifications for the tar-oil washes have been published by the United Kingdom government.[8a] The fraction boiling below 210° C is the light oil containing benzene, toluene, and xylene; that boiling between 210 and 240° C is the middle or carbolic oil containing the phenols and naphthalene; that boiling between 240 and 270° C is the heavy or creosote oil; and that boiling above 270° C is the anthracene oil.

Soaps

Soaps are the alkali salts of fatty acids. The soft soaps (the potassium salts) and the hard soaps (the sodium salts) are soluble in water; the calcium and magnesium salts, among others, are insoluble. The presence of these lime carbonates in hard water precipitates the dissolved soft or hard soaps. The principal value of soap as a detergent or emulsifier, wetter or spreader, lies in its capacity to reduce the surface tension of water. Soap solutions are used not only for their own insecticidal effect but

more especially for enhancing the toxicity of nicotine sprays for aphids; however, they are precipitated when admixed with lead arsenate and are also incompatible with calcium arsenate.

TABLE 8. Properties of Sodium and Potassium Soaps

	Soap Ester		Surface Tension of 0.1% Solution, dynes/cm	Per Cent Mortality of *Aphis rumicis*	Per Cent Hydrolysis of K Soap in 0.5 *N* NaOH
C_2	Acetate	CH_3COONa	....	..	0.03
C_4	Butyrate	C_3H_7COONa	64.7	..	.
C_6	Caproate	$C_5H_{11}COONa$	61.2	7	....
C_8	Caprylate	$C_7H_{15}COONa$	60.0	37	0.07
C_{10}	Caprate	$C_9H_{19}COONa$	49.3	55	0.08
C_{12}	Laurate	$C_{11}H_{23}COONa$	43.3	67	0.35
C_{14}	Myristate	$C_{13}H_{27}COONa$	26.6	30	0.54
C_{16}	Palmitate	$C_{15}H_{31}COONa$	57.6	25	0.63
C_{18}	Stearate	$C_{17}H_{35}COONa$	61.4	13	...
C_{18}	Oleate	$C_{17}H_{33}COONa$	35.0	85	...
C_{18}	Linoleate	$C_{17}H_{31}COONa$	39.4	.	.
C_{18}	Ricinoleate	$C_{17}(OH)H_{32}COONa$	48.7	..	....

Soaps are manufactured by alkaline treatment (saponification) of natural fats and oils, which contain a mixture of fatty acids, nearly all of which have an even number of carbon atoms. The main sources are linseed, cottonseed, rape, castor, coconut, soybean, palm, and corn oils, whale, cod, herring, menhaden, and sardine oils, neatsfoot oil, wool grease, and lard.[11] These oils were occasionally used as pest-control products but were soon replaced by mineral oils, which are much cheaper. As far as the soap is concerned, it was found that for maximum reduction of surface tension, maximum insecticidal activity, and a moderate susceptibility to hydrolysis the most effective fatty acids are in the neighbourhood of C_{12} or lauric acid (Table 8). The richest source of these fatty acids is coconut oil; the corresponding alcohols produced by reduction are also valuable as raw materials for contact insecticides, being produced under the name of *Lorol*.

Soaps are liable to hydrolysis by alkali, producing the metallic kation, and the fatty acid anion which remains on the colloidal soap micelles; the solution therefore becomes the more alkaline.

Soap is thus incompatible for use with alkali-labile insecticides such as pyrethrum or rotenone.

Synthetic detergents

The problem of insolubility in hard waters may be overcome by making a soap in which a sulphuric acid group is substituted for the carboxylic group, viz. R—OSO_3H instead of R—COOH. The sodium salts of these alkyl sulphuric acids are employed, and they are not rendered insoluble by kations which normally make for hardness. As in the true soaps, the bulk of the detergent molecule lies in the anionic component. Similar anionic detergents may be made from alkyl sulphonic acids, from aryl sulphonic acids, from alkyl aryl sulphonic acids,[12] and from sulphonic acid attached to the alkyl groups of esters and N-substituted amides. The surface-active properties of sulphite liquor are probably due to the lignin sulphonic acids. Non-ionic detergents may be made from the monoesters of fatty acids with polyalcohols, and from alcohol polyethers. Kationic detergents are rare and are known as "invert soaps."[88] The synthetic detergents may be dissolved in concentrated solutions of insecticides in oil, and these emulsion concentrates will emulsify themselves on dilution with water. Or they may be milled with insecticidal dusts to constitute wettable powders which will readily disperse in water suspension.

Detergents, Classed as Anionic

Sodium alkyl sulphates		
Dreft, Orvus WA	Na lauryl sulphate	Procter and Gamble
Duponol LS	Na oleyl sulphate	du Pont
Teepol X	Na secondary-alkyl (C_{10}-C_{18}) sulphates	Technical Products
Tergitol 4 and *Tergitol 7*	Na sulphate of higher secondary alcohol	Carbide and Carbon
Turkey Red Oil	NH_4 salt of ricinoleyl sulphate	
Sodium alkyl sulphonates		
Igepon A	Na salt of sulphonated ethyl oleate	General Dyestuff
Penetrol	Na salt of sulphonated oxidized petroleum oils	Kay-Fries Chem.
Aerosol OT, Vatsol OT	Dioctyl Na sulphosuccinate	American Cyanamid

Detergents, Classed as Anionic (*Continued*)

Sodium alkyl aryl sulphonates		
Santomerse D	Na decylbenzene sulphonate	Monsanto
Santomerse 3	Na dodecylbenzene sulphonate	Monsanto
Aresket 300	Na butylbiphenyl sulphonate	Monsanto
Nacconol NR	Na alkyl aryl sulphonate	National Aniline
Alkanol SA	Na alkylnaphthalene sulphonate	du Pont
Other sodium sulphonates		
Agral 2	Na salt of sulphonated aromatic hydrocarbon	I.C.I.
Igepon T	Na salt of sulphonated ethyl-oleylamide	General Dyestuff

Emulsifiers, Classed as Non-Ionic

NNO	Mannitan monolaurate	Atlas Powder
Span 80	Sorbitan monooleate	Atlas Powder
Tween 80	Polyoxyethylene derivative of sorbitan monooleate	Atlas Powder
Sterox CD	Polyoxyethylene condensate	Monsanto
Sterox SK	Polyoxyethylene thioether	Monsanto
R2204	Cetyl ether of polyethylene glycol	I.C.I.
Lissapol N	Octylcresol poly(C_8-C_{10})ether alcohol	I.C.I.
Igepal CA	Condensate of ethylene oxide and alkylated cresol	General Dyestuff
Triton X-45	Alkyl aryl polyethoxy ethanol	Rohm and Haas
Triton X-100	Alkylated aryl polyether alcohol	Rohm and Haas
Triton X-155	Alkyl phenoxy polyethoxy-ethanol	Rohm and Haas
Triton B-1956	Alkylated aryl polyether alcohol	Rohm and Haas

Invert Soaps, Classed as Kationic

Sapamine A	Diethylaminoethyloleylamide acetate	Ciba

Miscellaneous materials

Saponin, a glucoside from the soapwort *Saponaria officinalis*, has been occasionally used because it greatly reduces the surface tension. Casein reduces the surface tension of water and has been widely used as a spreader, besides being effective as a sticker. It is dispersed in water with the aid of 3 parts of lime (e.g. lime-casein, "calcium caseinate"). Gelatin and flour have also been used as wetting agents and adhesives. Blood albumin is often favoured as an emulsifier. Mention might be made of the synthetic adhesive, polyethylene polysulphide (*p.e.p.s*).

DUSTS

Dust diluents

Since dusting machines function efficiently only when delivering high volumes of material, powdered insecticides are diluted with finely ground minerals in order to reduce their cost and prevent wastage.[96] The most important are the silicates of aluminum or magnesium (e.g. talcs, pyrophyllites, bentonites, and clays). The diatomaceous earths, which consist mainly of silica (SiO_2), are also important. The properties and commercial sources of dust diluents have been published in a recent summary.[5] A general classification [122] is shown in Table 9.

TABLE 9. Classification and Properties of Dust Diluents [34,122]

			Bulk Density, lb/ft^3	Specific Gravity	Reaction, pH
Oxides	Silicon	Diatomite	9–11	2.0–2.3	5–8
	Calcium	Hydrated lime	28–32	2.1–2.2	12–13
Sulphates		Gypsum	49–57	2.3	7–8
Carbonates		Calcite	48–67	2.7	8–9
Silicates	1. Talc		30–52	2.7–2.8	6–10
	2. Pyrophyllite		28	2.7–2.9	6–7
	3. Clays	*a.* Montmorillonite	38–44	. .	9–10
		b. Kaolinite	30–35	2.6	5–6
		c. Attapulgite	27–31	2.6	7

Diatomite is a form of silica that is the principal constituent of the diatomaceous earths and kieselguhrs. Being essentially the skeletons of diatoms, these materials are highly spicular and exhibit a low bulk density. The *Celites* are ground to an average particle size of 4–9 μ and show a bulk density of 8–11 lb/ft^3. *Supercel* and *Santocel C* ("silica aerogel") are ground to a particle size below 1 μ and have a bulk density of 6 lb/ft^3. The uncalcinated gray *Celites* have a specific gravity of 2.00 and a moisture content of 6%; the flux-calcined white grades have less than 1% moisture and a specific gravity of 2.3. They contain up to 10% of impurities, mostly aluminum oxide. These materials usually have an acid reaction, though alkaline samples may be prepared. Diatomaceous earths are highly abrasive to the insect cuticle and alone can cause as much as 85% mortality

of beetles.[69] Silica may also be used in the form of the mineral tripolite found in tripoli clays.

Calcium oxides may be produced by roasting calcite or dolomite, but when used as dust diluents they may be expected to be in the slaked form of hydrated lime ($Ca(OH)_2$). Certain limes may contain more than 10% of MgO and are classed as magnesium limes. Hydrated lime is itself quite insecticidal, because it is decidedly alkaline and may saponify the insect epicuticle.

Calcite, or mineral calcium carbonate ($CaCO_3$), may be used in insecticidal dusts as ground limestone or whiting. It furnishes a slightly alkaline dust. Diluents may also be made from ground dolomite ($CaCO_3 \cdot MgCO_3$). **Gypsum,** or hydrated calcium sulphate ($CaSO_4 \cdot H_2O$), has been used as a dust diluent but is not favoured because it has a high bulk density.

Talc is essentially a hydrated magnesium metasilicate ($3MgO \cdot 4SiO_2 \cdot H_2O$). The ground dusts appear in a variety of forms: foliated or flat; spicular or fibrous; and granular or massive, when ground from soapstone or steatite. Talcs constitute about a third of the dust diluents now used. They show a great range in the *p*H reaction of various samples, many being considerably alkaline. With a few exceptions, talc dusts are not abrasive enough to be insecticidal in themselves.

Pyrophyllite is a hydrated aluminum silicate ($Al_2O_3 \cdot 4SiO_2 \cdot H_2O$) that is rather closely related to the clays. Being nonalkaline, it is especially favoured as a dust diluent for rotenone, pyrethrum, and chlorinated hydrocarbons. It is admixed with DDT when it is ground as a wettable powder. The usual varieties of pyrophyllite have flat or plate-like particles, and the laminae may be separated by heat: hence the name. Pyrophyllite itself is scarcely abrasive enough to be insecticidal.

Bentonite is a type of clay mineral whose principal constituent is montmorillonite ($Al_4Si_8O_{20}(OH)_4 \cdot xH_2O$). It exhibits the property of swelling with water, which meta- and sub-bentonite do not. It is able to hold nicotine and pyrethrin very tenaciously. The bentonites are not abrasive insecticides.

Kaolinite ($Al_4Si_4O_{10}(OH)_8$) is the principal mineral in China clays and kaolin clays. Other constituent minerals include nacrite, dickite, and anauxite. The particles may be flat to granu-

lar, but never spicular. These clay dusts are somewhat insecticidal. Another type of clay mineral is **attapulgite** ($Mg_5Si_8(OH)_6 \cdot 4H_2O$). The dusts (e.g. *Attaclay*) are often described as fuller's earths. They have fibrous or spicular particles and are quite decidedly insecticidal in themselves.

Elemental sulphur has also been used as a dust diluent for insecticides and is useful in that it is a miticide and fungicide itself. Finely ground botanicals have also been used as diluents for the sensitive pyrethrin and rotenone products. They include the flours of wheat, soybean, tobacco, walnut shell, wood, and pyrethrum marc, the ground flowers from which the pyrethrins have been removed.

The fineness to which a dust diluent has been ground may be determined by passing it through a series of sieves of various meshes and size openings. The finest sieves in the U. S. Standard Series are no. 325, with openings 44 μ wide, and no. 400, with 37 μ openings. These diameters, although just at the limit of the resolving power of the human eye, are too large to characterize insecticidal dusts, which are ground to much finer sizes.[18] Moreover, the finest particles of certain dusts (such as clays) refuse to pass these sieves in spite of being very much smaller than the sieve opening, and they require to be coaxed through by wetting; dry sieving therefore gives a false picture (see Table 10).

TABLE 10. Properties of Some Silicates Used as Dust Diluents[128]

Type (see Table 9)	Brand and Source	Mean Diameter by Surface, microns	Bulk Density, gm/cc	Specific Gravity	Per Cent through No. 100 Sieve	Per Cent through No. 325 Sieve
1.	Vermont talc	3.8	0.54	3.05	100	98
2.	*Pyrax ABB* (N. C.)	3.5	0.49	2.73	100	73
3b.	Brunswick clay (N. J.)	1.3	0.33	2.54	100	12
3b.	Cherokee clay (Ga.)	1.1	0.32	2.67	100	6
3b.	Topton clay (Pa.)	1.0	0.23	2.68	82	18
3b.	*Type 41* kaolin (S. C.)	0.6	0.21	2.58	97	4
3c.	*Attaclay* (Ga.)	1.9	0.29	2.59	99	47
3c.	*Diluex* (Fla.)	1.7	0.30	2.35	100	61

The dusts may be allowed to settle evenly on a glass slide and the individual particles measured under a microscope with the

aid of an ocular micrometer; from a sufficient number of values the arithmetic mean, the median diameter by number, or the median diameter by mass (m.m.d.) may be calculated. Since this is a tedious procedure, determinations have been made by the gas absorption, or, better, by the liquid or gas permeation method; this gives the mean diameter by surface area ($\propto d^2$) which is a figure lying between the number median ($\propto d$) and the mass median ($\propto d^3$). The air permeation method is based on the principle that a current of air flows less readily through a bed of fine particles than of coarse, even when the proportion of air space is identical, since the fine particles present a far greater amount of surface to oppose the viscosity of air. An apparatus called the *Sub-Sieve Sizer* has been developed whereby a sample of the dust, whose weight in grams is equivalent to its true specific gravity, is opposed to a flow of air under a constant pressure head, and the pressure difference across the sample is measured by manometer.[49] Dusts may now be adequately assessed by determining the surface-mean diameter to characterize them as a whole, and by using the no. 325 sieve to detect the small percentage of unsuitably large particles.

Effect of particle size on toxicity of dusts and suspensions

There is a large body of evidence to show that the toxicity of insecticides in particulate form steadily increases as the particle size decreases.[111] Paris green applied in suspension sprays and dusts against *Epilachna* shows a rising stomach toxicity as the particle size is reduced from 22 μ through 12 μ down to 1 μ, such that the amount necessary for a lethal dose with 1 μ material is approximately one-tenth that with 22 μ Paris green.[59] Similar results are obtained with the stomach toxicity of lead arsenate or cryolite to *Apis*.[19] With phenothiazine, toxicity rises steeply with fineness of grind.[108,131] The contact toxicity of pyrethrum in dusts and suspensions is significantly greater with fine particles than coarse; when dusted as a mosquito larvicide, the finest particles paralyse *Culex* within 10 min, whereas the coarsest take over 4 hr.[110] With DDT wettable powders, the toxicity of their deposits to *Musca* and potato flea-beetles is higher at 10–20 μ than at 25–35 μ.[112] It has been found that in-

creasing fineness of grind, down to 4 μ diameter, increases the toxicity of DDT deposits to the codling moth.[68, 113] Inert dusts, such as silica or alumina, do not become active insecticidally until they are finely ground down to 15 μ or smaller.[27]

When inert dusts of various minerals, of different particle size, are applied to a number of species of beetles, it is found that only those whose particle size is less than 10 μ are abrasive and thus insecticidal. More dust adheres to the insect, and more is ingested, if it is finely powdered.[32a]

However, other factors may enter to reverse this simple relationship of toxicity with comminution and consequent increase of surface. The smallest particles show less adherence to surfaces than those of moderate size; for example, in the range from 1 to 22 μ, less Paris green was retained on bean leaves in the case of the smaller particles.[89] The tenacity of DDT applied for codling-moth control was reduced as the particle size was decreased.[113]

Another factor is that the finest particles either fail to be deposited in the target area [92] or may pass right through a canopy of foliage without depositing upon it.[2] Extremely fine dusts were found to be generally inferior diluents for derris powders.[119] And when lead arsenate, cryolite, or Paris green suspensions were applied to apple plugs for *Carpocapsa* control, the finest (2–4 μ) particles proved to be less effective than the moderately fine (8–18 μ) and were no better than the 30 μ particles.[108] In some cases the finest particles may be of a different chemical nature from the coarsest; with calcium arsenate dust, the finest particles are composed of the less toxic basic salt, the more toxic acid salt being confined to the coarser particles.[112]

There is also good evidence that a certain size and shape are necessary for uptake of a residual contact insecticide such as DDT on the insect body. Whereas a film of liquid solvent in which there is a supersaturated solution of DDT does not show a very high residual toxicity to houseflies because it is not taken up by the insect body, crystallization of the DDT from this solution results in a regeneration of the residual toxicity of the deposit,[94] since the needle-like crystals may be broken off to adhere to the fly's limbs. For the same reason, deposits from

emulsions of DDT show far less residual toxicity to young *Grapholitha* larvae than those from wettable powders or dusts.[81a] And so it is found that if DDT crystals of various sizes and shapes are prepared in 0.1% aqueous suspension, and adult *Tribolium* are dipped into them, the maximum toxicity is shown by those crystals which show maximum retention on the spines and crevices of the body. Similar results are obtained by spraying the suspensions onto *Tribolium*, although naturally the larger needles are broken up in the act of spraying. Thus needle-shaped crystals are more effective than plate-like crystals, and longer needles are more effective than shorter ($400\ \mu > 120\ \mu > 40\ \mu$). Similarly the larger crystal plate aggregates ($240\ \mu \times 140\ \mu$) are more effective than the smaller ($60\ \mu \times 15\ \mu$), and colloidal particles are by far the least effective.[86] This may be one of the reasons for the poor showing of commercial preparations of "colloidal DDT" as compared with the conventional wettable powders.[77]

As far as the globule size of the oil phase in emulsions is connected with its toxicity, the evidence is contradictory. For the control of armoured scales, it has been reported that the efficiency increases as the oil is reduced below 5 μ globule size.[18] Yet for the control of aphids with lube-oil or gas-oil emulsions, those with 10 μ globules were found to be more effective than those with 2 μ globules, since the larger globules resulted in a higher deposit on the foliage.[52] It has been concluded for similar reasons that coarse, quick-breaking emulsions are superior, since the water quickly runs off without taking the oil with it, but instead leaves it as a continuous film.[35] The balance of opinion is that globule size *per se* has no relation to the toxicity of insecticides in emulsions; this is decided by other properties of the emulsion, which may incidentally affect the globule size.[38] Water-in-oil or invert emulsions are not used in insect control, since they cannot be sprayed.[78] But a system may be made of oil, water, soap and an inorganic insecticide, wherein the suspended insecticide shows an affinity for the oil phase, and on being sprayed forms a curd which can accumulate on the point of deposition. Such systems have been called "inverted spray" mixtures [83] or "oil-flocculated" mixtures.[39]

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CHAPTER II

The Structure of Organic Chemicals and Their Toxicity to Insects

Introduction

The search for insecticidal compounds, which was greatly accelerated during World War II, continues to advance into the fertile fields pioneered by the organic chemist. As a result, insecticides of ever greater power are being discovered, and the arsenal of weapons for insect control is steadily increasing.[74] This is not simply a process of multiplying the number of insecticides that are redundant to each other; for each new compound exhibits its own pattern of physical properties, which imparts a certain selectivity of action against various species of insects. These differences in species susceptibility may be discovered by laboratory and field testing, and careful investigation may establish their relationship with the physical and biological properties of the chemical compound. In this way insecticides may be

developed to be aimed against specific insect targets, and the use of more general poisons may be avoided.

Information on the insecticidal activity of some 10,000 compounds, nearly all of which are organic chemicals, is now available in the open literature.[14] It is probable that the number tested by private corporations, the results of which have not been divulged, amounts to several times this figure. From this vast array, some 10 compounds have found general use as effective insecticides, and approximately 100 compounds are being employed for restricted purposes or are still in the process of development.

In attempting to derive clues as to the relation between molecular structure and toxicity, the student is baffled by the prolixity of the test methods employed by different workers, and the terms in which the results are expressed. Tests for insecticidal activity may involve the operation of stomach, fumigant, injection, contact, or residual toxicity, or a combination of conditions where more than one of these modes of action may operate simultaneously. It is important to assess these types of toxicity separately, because the properties making for a good fumigant, for example, may differ considerably from those of a good contact insecticide. The species used as test animals vary, as also the stage, whether larva, nymph, or adult. However, there is a preference for certain test insects,[21a] namely nymphs of *Blattella*, *Oncopeltus*, *Aphis*, or *Pediculus*; larvae of *Bombyx*, *Prodenia*, *Carpocapsa*, *Musca*, *Cochliomyia*, *Culex*, or *Anopheles*; and adults of *Sitophilus*, *Tribolium*, *Musca*, or *Drosophila*.* The toxicity of a given compound will be found to show considerable variation, depending on the species employed and its stage of development.

One of the greatest difficulties lies in the interpretation of the results of tests for toxicity. Since the relation of structure to insecticidal activity is best followed by observing the effect on toxicity of unit changes in molecular architecture, the toxicity should be expressed in quantities which may be used comparatively. The mortality figures for a single concentration are

* The full technical nomenclature, along with the common names of these insects, is given in a list at the end of this chapter.

nearly always inadequate, especially when they are at a level above 90% or less than 10%. It is necessary to obtain mortalities at a sufficient number of concentrations to establish the median lethal concentration, deposit, or dosage. In addition to the level causing 50% mortality (LD_{50}), that causing 95% kill (LD_{95}) is a useful figure to determine for practical purposes.

A consideration of the general picture yielded by the results of toxicity testing reveals that it is impossible to predict the type of molecule that might be an effective insecticide. However, a number of trends may be discerned in the relation of chemical structure to insecticidal activity. These may be summarized as follows:

1. The best contact insecticides are of a certain size. The molecular weights of pyrethrins, rotenone, DDT, toxaphene, chlordane, lindane, and many others are approximately 300–400. A study of DDT analogues showed that maximum toxicity occurred at molecular weights between 300 and 450 m.w.[96] With the exception of rotenone, the best insecticides contain only one or two rings of carbon atoms. All the derivatives of indane ($C_5 + C_6$ fused ring system) that have been tested showed insecticidal activity.[46] Derivatives of anthracene, phenanthrene, and chrysene, with three or more rings, are of inferior toxicity. Thus it would appear that there is an upper limit to which the synthetic chemist can profitably build his molecules.

2. Certain substituents confer toxicity on the molecules to which they are added. The outstanding toxic groups are as follows: (*a*) Halogen (principally Cl), as in DDT, lindane, chlordane, aldrin, toxaphene, propylene dichloride, and methyl bromide; (*b*) SCN (thiocyanate), as in the *Lethanes* and *Thanite*; (*c*) NO_2 (nitro), as in DNOC, DNCHP, *DN289*, *Ethide*, and parathion; and (*d*) CN (nitrile or cyanide), as in HCN, acrylonitrile, and phthalonitrile.

a. Among 1054 chlorinated compounds that have been tested for their insecticidal properties, it was found that 87.3% of the monochloro derivatives were active, the figure rising steadily with increasing chlorination to 95.5% activity with the pentachloro compounds.[46] Increasing chlorination of the ethane side-chain of the analogues DDT and *p*-chloroethylbenzene, up to a point, increases their insecticidal efficiency.[176] From a study of the effect of DDT analogues on arthropod nerve, it has been considered that chlorination of the molecule increases its toxicity by increasing the molecular density, thus making it less susceptible to removal from the receptor it blocks.[200] However, it must be pointed out that chlorination of the ethane nucleus of *p,p'*-dichlorophenylethanes decreases their acaricidal effectiveness.[113] It has been considered that the toxophoric properties of chlorine or other halogens

depend on their susceptibility to dehydrohalogenation, with the production of HCl or other halogen acid.

b. Of 112 thiocyanates that have been tested, 97.6% showed insecticidal activity; this is the highest frequency of toxicity to be found for any substituent group.[46] Of 36 isothiocyanates tested, 94.5% showed some measure of activity.

c. The toxicity of the three dinitro insecticides mentioned above is a special case; it depends on the position of the nitro groups on the benzene ring, where one is in a position *para* to a phenolic group, the other being *ortho* to it and balancing an alkyl substituent. When nitro compounds as a whole are considered, they are found not to show a high frequency of toxicity, being limited to 72.0% for mononitro, 65.2% for dinitro, and 61.5% for trinitro compounds.[46]

d. Of the 45 mononitriles tested, only 68% showed insecticidal activity, but all of the 6 dinitriles proved to be toxic.[46]

3. Certain substituents reduce the contact toxicity of the molecule. The most conspicuous examples are the highly polar and acidic carboxyl (—COOH) and phenolic hydroxyl (—OH) groups. It has been postulated that their polarity prevents their passing through the insect cuticle; instead they are anchored on it by chemical reaction. It is noteworthy that the excellent contact insecticide DDT is completely apolar.

4. Amino and amido groups, which are highly polar, appear to reduce the chances of compounds proving toxic. The disubstituted primary, secondary, and tertiary amines show a low incidence of insecticidal effect, as also do the unsubstituted amides. Even the azo compounds and semicarbazones, although they include a few quite good insecticides, as a group have a low proportion of active compounds.[46]

5. Certain substituents aid contact toxicity by conferring or increasing lipoid solubility, such as the methoxy ($CH_3O—$), methyl ($CH_3—$), and analogues, ethylene ($—CH_2—CH_2—$) and chloroform (as in $—CH—CCl_3$) groups, and the benzene, cyclopropane, benzofuran, and benzopyran rings. It is probable that the question of optimum length of aliphatic side-chains is related to liposolubility. For contact toxicity, it would appear that the optimum alkyl substituent depends on the size of the nucleus of the molecule. Where the nucleus is very small, the optimum length is about C_{12} (e.g. lauric acid, sodium laurate, lauryl thiocyanate). Where it is of moderate size, the optimum is C_5–C_8 (e.g. 2-heptylpyridine, 2-valeryl-1,3-indandione, 6-heptyl-2,4,-nitrophenol). Where it is large, such as the diphenyl-trichloroethane nucleus, the optimum size is C_1 or C_2, as in methyl- or ethyl-DDT. For fumigant toxicities the optimum lengths, even with small nuclei, are considerably smaller.

6. Unsaturation in an aliphatic side-chain increases toxicity. This effect may be observed in the aliphatic hydrocarbons and fatty acids and in the side-chains of pyrethrins, rotenone, and piperine. The allyl ($CH_2{=}CH—CH_2—$) and crotonyl ($CH_3—CH{=}CH—CO—$) radicals are highly effective substituents.

7. When the toxic grouping is attached to a benzene ring, its toxicity is best enhanced by further substitution in the *para* position (e.g. *p*-aminophenyl thiocyanate, *p*-bromo-N-ethyl-benzenesulphonamide, *p*-chlorophenyl chloromethyl sulphone). This holds good for the diphenyl sulphides, sulphoxides, sulphones, and ethers, and for the analogues of DDT. The *ortho* position is occasionally as good or even better than the *para* when OH, NO_2, and NH_2 groups are concerned (e.g. *o*-nitroaniline, 2,4-dinitro-*o*-cresol, N-methylpicramic acid). *Meta*-substituted benzene derivatives are, with few exceptions, of negligible toxicity.

8. The molecular structure of many insecticides resembles that of bactericides and fungicides in containing a carbonyl (C=O) group attached to an ethylenic double bond, resulting in the toxophoric C=O—C=O configuration. This is found in the cyclic insecticides: pyrethrins, rotenone, valone, xanthone, and piperine; and the configuration is present in the aliphatic fumigants acrolein, crotonaldehyde, and mesityl oxide, and the esters ethyl acrylate, allyl formate, diallyl succinate, and diallyl fumarate.

9. Many good insecticides contain ether (—O—) linkages, such as dichlorodiethyl ether, bis(fluoroethoxy) methane, butylcarbitol thiocyanate (*Lethane 384*), and the synergist piperonyl butoxide. Of 975 compounds containing monoether linkages that have been tested, 92.9% showed some insecticidal activity; of 397 diethers, 93.2% were insecticidal.[46] The cyclic ether linkage known as a lactone ring is common to rotenone, xanthone, and derivatives of coumarin, and two cyclic ether linkages are found in the synergistic methylenedioxyphenyl derivatives.

It is evident that the relation of molecular structure to insecticidal toxicity is not a simple one. The factor of cuticle permeability in a contact insecticide, and of adsorbability in a fumigant, is superimposed upon the metabolic or enzymic toxicity of the compound. It would appear reasonable to consider that different groups of compounds must have different physiological and biochemical effects. Certain of the nerve poisons (organic phosphates, fluorides) are inhibitors of the enzyme cholinesterase, which is necessary for the maintenance of synaptic conduction. Yet other insecticides (DDT, nicotine, thiocyanates) are nerve poisons without being anticholinesterases. Certain fumigants (methyl bromide, narcotic vapours) act as inhibitors of dehydrogenases by attacking the SH groups of these enzymes; others (hydrogen sulphide, hydrogen cyanide) are inhibitors of cytochrome oxidase by attaching to its Fe group. It has also been found that certain poisons containing the C=C—C=O configuration also act on the SH groups of tissue dehydrogenases.

It has been considered by many workers that the shape of the molecule is of outstanding importance. There is evidence that

a symmetrical or umbrella-shaped molecule is more likely to block the tissue receptors than an asymmetrical one.[13] Many of the best insecticides have a symmetrical molecular structure, of which DDT is the best example. Other structurally symmetrical insecticides include *p*-dichlorobenzene, azobenzene, and diphenylamine; (*p*-chlorophenyl) sulphides, sulphoxides, and sulphones; tetramethyl thiuram disulphide; methoxychlor, DFDT and DDD; dichloroethyl ether, bis(*p*-chlorophenyl) ether and bis(fluoroethoxy) ethane; TEPP, tetrakis(dimethylamino) pyrophosphate, and parathion. Nevertheless, many extremely powerful insecticides are asymmetrical, for example aldrin, dieldrin, chlordane, toxaphene, the pyrethrins, rotenone, and nicotine.

Research into the relation of toxicity to the structure of analogues of the best insecticides (pyrethrins, rotenone, nicotine, DDT) has elucidated the effect of unit changes in the molecule on its toxicity. In many cases a small change in substitution, saturation, or arrangement has been found to exert an identical effect on toxicity in widely differing compounds; in this way toxic groupings may be treated as being additive. However, it is not yet possible to build up *ab initio* a molecule which can be predicted to be insecticidal.

Aliphatic hydrocarbons

The saturated hydrocarbons of the paraffin series are characterized by slight toxicity. Thus their effect on insects is decided more by their physical characteristics than by specific toxicological action. In the lower range of the series they show a moderate fumigant toxicity characteristic of narcotic vapours. An increase in effectiveness may be noted in the series pentane < hexane < heptane, decreasing again in octane.[152, 186] However, a saturated atmosphere of decane is sufficient to kill *Sitophilus* adults.[11a] The higher analogues are not sufficiently volatile to show fumigant action.

The lower members of the series do not show contact toxicity because they are too volatile, but contact toxicity begins to appear in the paraffin oils which are used as solvents for insecticides. In sprays for the housefly, a heavy kerosene gives quicker knockdown and higher kill than a light grade.[19] Finally ex-

cessive viscosity will set a limit to this increase in toxicity. However, it has been found that the rise in contact toxicity of saturated paraffins to insect eggs is not gradual, like the decline in volatility or the increase in viscosity, but shows an abrupt rise from oils with an average molecular weight of 270 (C_{19}) to those with a molecular weight of 340 (C_{24}), beyond which point it shows no further increase[134] (Fig. 1).

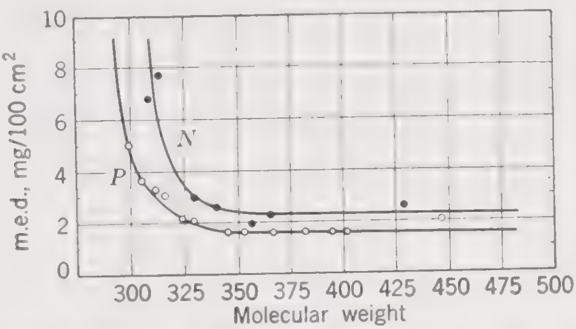


FIG. 1. Molecular weight of saturated hydrocarbons and their toxicity to *Grapholitha* eggs (as indicated by the minimum effective dosage). *N*. Naphthenic series. *P*. Paraffinic series. (From Pearce, Chapman, and Frear)

The unsaturated aliphatic hydrocarbons (olefins or alkenes) are very much more toxic than the saturated paraffins. They are responsible for a great deal of the toxicity of unrefined paraffin oils; since the removal of the unsaturated compounds by sulphonation from a toxic kerosene results in medicinal paraffin, which is non-toxic to insects. The saturated aliphatic compounds are 50% more toxic than the naphthenes (saturated cyclic hydrocarbons) of corresponding molecular weight,[134] according to tests with caterpillar eggs, with mites, and with eggs and nymphs of scale insects. However, the aliphatic hexane is less toxic as a fumigant than benzene, which is equitoxic with heptane.[186]

Aliphatic alcohols

The alcohols as a group are not very powerful insecticides, but they are capable of inducing a narcosis which may be fatal. It has been found that their narcotic activity for *Phormia* larvae, as measured by the reciprocal of the threshold molar concentration required to induce paralysis, increases with their molecular

weight.[71] Aqueous sprays containing sufficient concentrations of the aliphatic alcohols are toxic to *Myzus persicae*.[131] Their effectiveness, molecule for molecule, rises as the series is ascended from propyl to octyl alcohol, each succeeding member being approximately 2.6 times as toxic as the preceding one, when the reciprocal of the median lethal molar concentration is taken as the index of toxicity (Fig. 2). The peak of activity is reached with lauryl alcohol, which shows high contact toxicity to aphids. The higher members of the series, such as cetyl and oleyl alcohols, show a decrease in contact toxicity associated with reduced cuticle permeability due to their higher capillary activity.[74] It is probable that a decrease in molecular motility, reflected in greatly decreased volatility and increased viscosity, is also a factor.

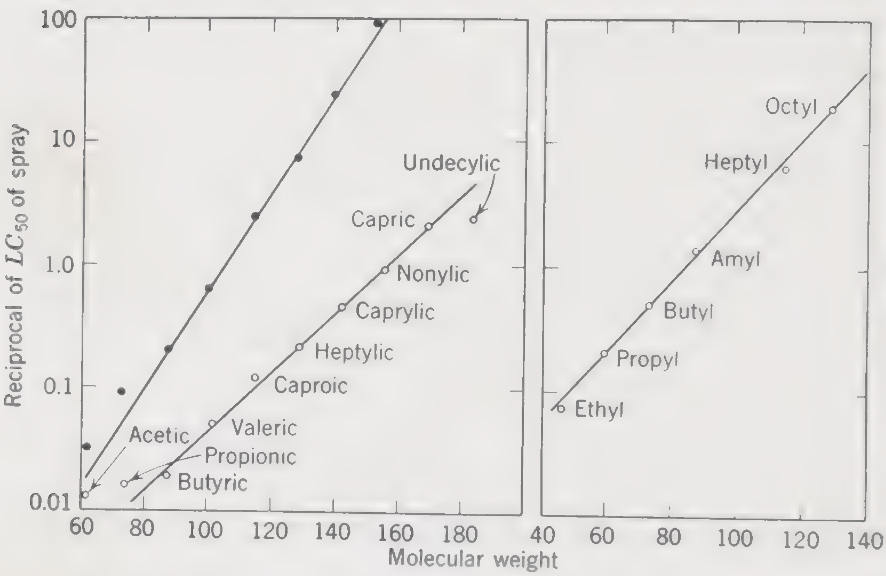


FIG. 2. Molecular weight of fatty acids and aliphatic alcohols, and their contact toxicity to *Myzus*. (From O'Kane *et al.*)

It is a general observation that the power of compounds in a series to induce narcosis in living matter increases as the homologues of higher molecular weight are employed. This was interpreted by Overton and Meyer[132] to be due to the fact that as the hydrocarbon chain (whether of alcohols, fatty acids, amines, or aldehydes, etc.) was lengthened, the lipoid solubility of the molecule, or rather its partition coefficient lipoid/water, increased. Thus it would have a stronger tendency to enter the lipoid nerve

sheaths and narcotize the organism. This view has received confirmation in more recent work with surface films of lipoid on water, where the ease of penetration of the compound into the monomolecular layer, and incorporation in it, was found to increase with the length of the hydrocarbon chain.[150]

On the other hand, the increase of narcotic activity with molecular weight in a homologous series was interpreted by Traube as being correlated with the increase in surface or capillary activity, as measured by the power of each member to lower the surface tension of water.[193] Traube's rule states that the concentrations at which equal lowering of the surface tension is obtained diminish threefold for each additional carbon atom in the hydrocarbon chain.[1] And in experiments with members of a homologous series it is found that the molar concentration required for equal effect is approximately one-third of the concentration required of the preceding member.[3] This is also the case in the contact insecticidal effectiveness on *Myzus* mentioned above.[131] The power of an aliphatic alcohol to inhibit liver lipase proves to be approximately 3 times that of its preceding homologue.[79] The narcotic activity of alcohols increases with their power to lower surface tension. It has been found that this relationship holds good for the inhibition of respiration in the eggs of the sea-urchin *Arbacia* by members of the alcohol series even when the tissue has been extracted of its fat.[150]

The increase in the power of higher analogues of any given series to produce the same effect at lower molar concentrations does not proceed indefinitely. At some point in the ascent of the homologous series the increase in biological activity ceases and reverses. The position of this cut-off in the activity of the series is a characteristic of the particular chemical series and the biological effect which it produces. In some cases this may be attributable to purely physical characters, such as viscosity, volatility, and solubility. Where these do not apply, it has been suggested that the position of this cut-off is decided by the point at which the thermodynamic activity of the chemical in solution approaches unity[3] (see below). With fumigant vapours for *Sitophilus*, this occurs at butyl alcohol, above which even saturated atmospheres do not kill.[41a]

Fatty acids

The activity of fatty acids as contact insecticides rises as the series is ascended. The contact toxicity of a series of acids from butyric (C_4) to capric (C_{10}) for *Aphis rumicis* was found to increase by a factor of approximately 2.2 for every additional carbon atom in the chain.[158] This increase in toxicity closely parallels the increase in the surface activity of the acids (Fig. 2). With larvae of *Phormia* or *Calliphora* it has been found that the toxicity of fatty acids, as measured by the threshold molar concentration for paralysis, does not increase with molecular weight but remains constant, although the cuticular penetration, as measured by the rate of kill, increases as the series is ascended from caproic acid (C_6).

When the homologous series of fatty acids is ascended still farther, it is found that maximum toxicity is reached in the vicinity of capric (C_{10}) and lauric acids (C_{12}). Fatty acids applied as sprays to *Anuraphis* showed no great toxicity below valeric, a steep ascent to a peak at capric, and a gradual decrease from lauric through myristic and palmitic to stearic (C_{18}) acid.[169] The best source of these compounds is found in coconut fatty acids, which contain 50% of lauric acid. Similar tests with *Aphis rumicis* revealed that the peak occurs at undecylic acid and the toxicity beyond tridecylic acid is slight: the unsaturated oleic acid is considerably more insecticidal than the saturated stearic acid. The correlation of toxicity with lipoid/water partition coefficient on the Overton-Meyer basis is exact as far up the series as decylic acid; but for higher analogues it breaks down, the absolute lipoid solubility of myristic, palmitic, and stearic acids being very low. However, the relation between surface activity and toxicity continues to be exact in this region, for the higher fatty acids have not sufficient mobility to reduce surface tension within a reasonable period of time (about 30 min), and thus their surface activity decreases in a fashion parallel with their toxicity.[186] The toxicity of the analogous phenyl-alkyl acids to bacteria is also most closely correlated with their surface activity.

Whereas the most toxic even-numbered fatty acid, applied in emulsion to *Aphis rumicis*, is capric acid (C_{10}), the most toxic soap applied in solution was found to be the potassium salt of

lauric acid (C_{12}). In the latter case, toxicity is most obviously correlated with the capacity of the soap to spread the deposited solution over the cuticle of the insect. The surface tension and the angle of contact were minimal in the case of the laurate soap, ensuring excellent spreading, whereas with the caprate they were twice as great [36] (Table 1). The sodium salt also of lauric acid was found to give the lowest contact angles both on *Tenebrio* cuticle and on paraffin-coated slides.[130] The superior surface activity of lauric acid is probably an important factor in the effectiveness of thiocyanoethyl laurate as a knockdown contact poison. It is nevertheless probable that a superior cuticle permeability, consequent upon liposolubility, is also a main factor in the contact efficacy of lauric acid and laurate esters and of lauryl thiocyanate and lauryl cyanide.

TABLE 1. Toxicity of Fatty Acids and Their Soaps to *Aphis rumicis* [36]

Fatty Acid	Free Acids, % Mortality	Potassium Soaps		
		% Mortality	Surface Tension *	Angle of Contact
Caproic	15	17	71	93
Caprylic	18	37	62	..
Capric	45	55	37	84
Lauric	42	67	20	42
Myristic	17	30	29	..
Palmitic	15	25	36	72
Stearic	11	13	45	85
Oleic	19	85	23	33

* In dynes per centimetre for 0.5% solution.

Alkyl side-chains

Since the molecules of most insecticidal compounds contain alkyl groups, whether they are long as in the soaps or thiocyanates, or short as in DNOC or organic fumigants, it is important to know whether their toxicity may be enhanced by changing the length of the alkyl side-chain. The relationship between toxicity and chain length has been investigated quantitatively for the alkyl-pyridines, the primary and secondary aliphatic amines, and the 6-alkyl-2,4-dinitrophenols.

The effect of the length of the alkyl group substituted in the 6 position on the 2,4-dinitrophenols has been investigated with

reference to their stomach toxicity to *Bombyx* larvae[77] (Table 2, column 6). The first member of this series, where R is a methyl group, is the insecticide DNOC. It was found that the toxicity increased with chain length to reach a peak where R was hexyl or heptyl, and the toxicity was 12 times greater than that of DNOC. With alkyl side-chains added as ethers to pentachlorophenol, it was found that the toxicity increased from methyl to amyl and thence decreased to dodecyl pentachlorophenyl ether.[199]

The effect of the length of the acyl groups substituted on the 2 position on the 1,3-indandiones has been investigated with respect to their contact toxicity to *Musca*.[80] The toxicity increases when the chain length increases from C_2 (acetyl) to C_5 (valeryl, isovaleryl, or pivalyl), and decreases with greater length of aliphatic chain or with aromatic substituents. The isovaleryl and pivalyl-indandiones constitute, respectively, the insecticides valone and *tert*-butyl valone.

TABLE 2. Relation of Toxicity to Length of Side-Chain

	Pyridines *		Amines		2,4-Dinitrophenols §
	2-Alkyl	4-Alkyl	Primary †	Secondary ‡	6-Alkyl
Ethyl	3.5	4.1	..	..	29
Propyl	7.0	14.0	..	..	18
Butyl	10.1	37.9	20	..	9
Amyl	34.2	79.8	36	7	8
Hexyl	68.7	99.2	..	58	4
Heptyl	98.2	....	51	73	4
Octyl	97.4	....	..	77	10
Decyl	....	....	..	12	..

* Per cent control from 1% spray on *Aphis rumicis*.[83]

† Per cent mortality of *Musca* larvae in $\frac{1}{8}$% of the compound ($\frac{1}{2}$% for butylamine).[72]

‡ Per cent mortality of *Musca domestica* adults.[31]

§ Median lethal dose (stomach) in micrograms per gram for *Bombyx mori* larvae.[77]

The toxicity conferred on pyridine by side-chains of varying length has been investigated by comparing them as fumigant vapours on *Tribolium* adults, and as contact sprays for *Aphis rumicis* (Table 2). Here the alkyl group may be substituted in

the 2 or the 4 position on the pyridine molecule. For fumigant effect on *Tribolium*, maximum toxicity is obtained with the 2- and 4-propyl pyridines.[82] For contact effect on *Aphis*, maximum toxicity is obtained when R is heptyl in the 2-alkyl series, and when R is hexyl or higher in the 4-alkyl series.[83] Thus, for maximum contact activity, alkyl pyridines require a longer side-chain than for maximum fumigant action. Of the alkyl esters of picolinic acid, the hexyl is the most aphicidal and the decyl the most ovicidal.[22a]

Investigation of the general toxicity of primary amines to *Musca* larvae indicates that it increases in ascending to *n*-heptylamine and falls off in the higher analogues [72] (Table 2). Similarly, the contact toxicity of secondary amines to *Musca* adults attains its maximum effect at di-*n*-octylamine, with a sharp drop to di-decylamine (Table 2). If the two alkyl substituents on the amino group differ by more than 1 carbon atom in length, the toxicity is greatly reduced as a result of the asymmetrical form of the molecule. Branched alkyl groups are less toxic than straight chains, and their toxicity follows the length of the longest chain in the branched system.[31] With larvae of *Musca*, however, the optimum chain length for secondary amines appears to be C_4 (dibutyl) or less. The same picture is shown by alkyl-substituted thioureas, where the most toxic member of the series is mono-*n*-butyl thiourea, which is almost as toxic as thiourea itself.[72] It would appear that the larger the nucleus of the molecule, the shorter is the optimum length of side-chain. In the case of diphenyl-trichloroethane, which is a large molecule, the optimum alkyl derivative is methyl-DDT, and the optimum alkoxy derivative is methoxychlor.

Toxicity and boiling point of fumigants

Studies on the fumigant toxicity to insects of a long series of volatile organic compounds have revealed a tendency for the least volatile compounds to show the lowest values for median lethal concentration (LC_{50} or m.l.c.). On the other hand, the more volatile compounds require the higher concentrations, in terms of milligrams of vapour per litre of air, to obtain the same degree of mortality. Thus it has been pointed out that there is a gen-

eral relationship between the fumigant toxicity of a compound and its boiling point.[70, 120]

This relationship becomes erratic with compounds whose boiling points exceed 200° C.[190] Compounds with a boiling point above 240° C show an apparent drop in toxicity, since a high proportion of the fumigant is wasted by being adsorbed on the walls of the container or by failure to volatilize in the first place. In order that these compounds of very low vapour pressure may exert a fumigant toxicity, it is necessary to add them to the container in amounts exceeding the figure theoretically needed to saturate the air. If excess material is added, kills may be obtained with vapours from compounds of as low volatility as lindane (vapour pressure 0.07 mm Hg at 25° C) and chlordane (vapour pressure 1×10^{-5} mm Hg).

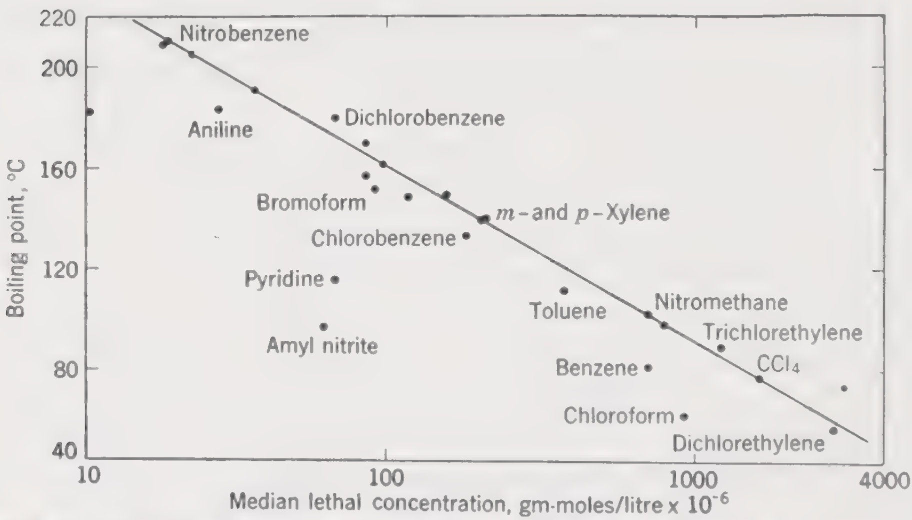


FIG. 3. Relation of boiling point of fumigants to their toxicity to *Agriotes* larvae. (Data of Tattersfield and Roberts)

If the toxicity as represented by the m.l.c. or LC_{50} in gram-moles per litre is compared with the boiling point of the compound in degrees centigrade, the existence of an inverse relationship becomes evident. When the LC_{50} values are plotted on a logarithmic scale (since toxic action is logarithmic) against the figures for boiling point on an arithmetic scale, it will be found that the points obtained for most of the compounds fall on a straight line. This is well demonstrated by a series of tests on

Agriotes larvae (Fig. 3), where the slope of the linear relationship indicates that the LC_{50} decreases, or the toxicity increases, 10 times for every 70° rise in boiling point of the compounds concerned.[130] Results obtained on *Musca*[120] indicate a similar tenfold increase in toxicity for a rise in boiling point of 78°, and tests of a series of compounds on *Tribolium*[9] indicate a tenfold increase for every 73° rise in boiling point.

If toxicity bears this inverse relation to boiling point, it must bear a direct relation to the vapour pressure and to the volatility (rate of evaporation) of the compound concerned. Indeed, it has been found that the fumigant toxicity of a series of compounds to houseflies is in direct proportion to their rate of evaporation from glass plates[121] (Fig. 4). The relation between the boiling point of a compound and its fumigant toxicity is quite similar to that between boiling point and vapour pressure. Whereas the vapour pressure decreases tenfold for every 50° rise in boiling point, the fumigant toxicity increases tenfold (on the average) for every 75° rise in boiling point.

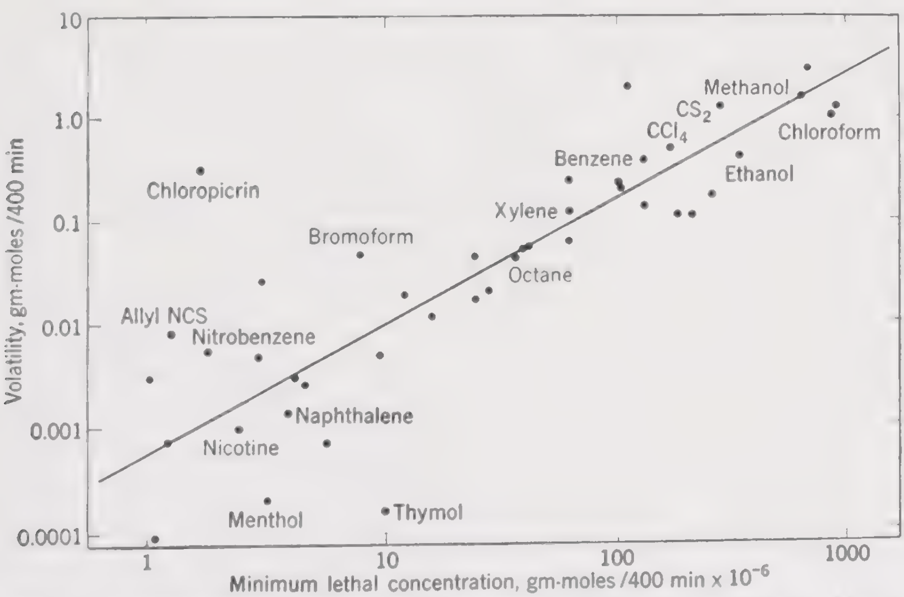


FIG. 4. Relation of volatility of fumigants to their toxicity to *Musca* adults. (Data of Moore)

This discrepancy may be elucidated by considering the air-saturation values of the series of compounds that are tested as

fumigants in glass vessels. The molar concentration of vapour required to saturate air at S.T.P. is a direct function of the vapour pressure. From consideration of a number of compounds falling on the line relating toxicity to boiling point, and extending over a range of vapour pressures (Fig. 5), it may be seen that the more volatile compounds (vp. > 10 mm Hg) show an m.l.c. to *Tribolium* which is roughly equivalent to one-third of their saturation value. Those with vapour pressures between 1 and 10 mm Hg show m.l.c.'s between 50 and 90% of their saturation value, while the compounds of low volatility and high boiling point (v.p. < 1 mm Hg) show apparent m.l.c. values which are greater than the saturation value. This may be an artifact, due to adsorption on the walls of the glass vessel making the concentration of vapour appear larger than it actually is. The ability of glass vessels to remove vapours from the enclosed air to give misleading results is notorious.[198]

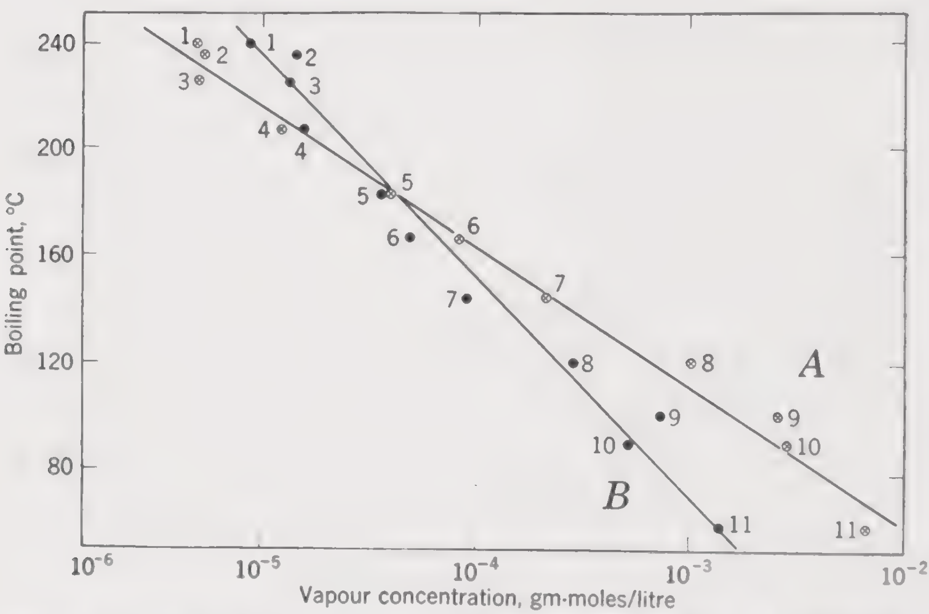


FIG. 5. Relation between toxicity and saturation value of fumigants. ● Median lethal concentration for *Tribolium* adults. ⊗ Concentration at which the air is saturated with the vapour. Fumigants are numbered from 1 to 10. (For legend see Brown, 1949.)

It has been argued that the increase in toxicity is attributable to the ascent of a homologous series of compounds, and that

therefore both the toxicity and the boiling point will rise as the molecular weight increases. However, the relation of fumigant toxicity to the molecular weight of compounds is much less close than to their boiling points. Therefore, too, the rate of diffusion is not a limiting factor.[190] And the toxicity-boiling point relationship is followed by a great variety of organic compounds irrespective of their molecular weight or molecular structure. Since toxicity is a consequence of volatility as indicated by boiling point, the peak will be reached when the boiling point is too high for effective volatility.

It is possible that the fumigant toxicity of the less volatile fumigants may be enhanced by their higher adsorption potential. During the exposure period, the vapour is adsorbed as a condensed film on the tracheal walls and the outer cuticle, and absorbed into the tissues; these two processes together have been named "sorption." The adsorption potential, which is essentially the work-resisting desorption or revolatilization, increases as the volatility of the compound decreases.[118a] Being an index of condensability, it bears a closer relation to the critical temperature (the temperature above which the vapour of the compound cannot be liquefied) than to the boiling point.[90] Since the low-vapour-pressure compounds of high adsorption potential resist desorption more effectively, they remain with the insect for a longer period of time after fumigation has been completed. Thus their desorption may proceed so slowly that the insect may succumb before the poison has been eliminated.[121, 190]

When all is considered, it is evident that the relation between the boiling point of fumigants and their toxicity to insects is primarily a relation between the boiling point of the compound and its consequent vapor pressure. The factor of adsorption will produce experimental artifacts which prevent this relationship being apparent for the less volatile fumigants. All those compounds whose vapours kill at approximately the same relative saturations (not less than 10% of the vapour saturation figure) will therefore fall on this linear relationship or close to it. It is found that the majority of vapours kill insects at relative saturations between 10 and 100%, i.e. at toxic thermodynamic activities between 0.1 * and 1.0, and it is considered

* A relative saturation of 10% implies a thermodynamic activity of 0.1.

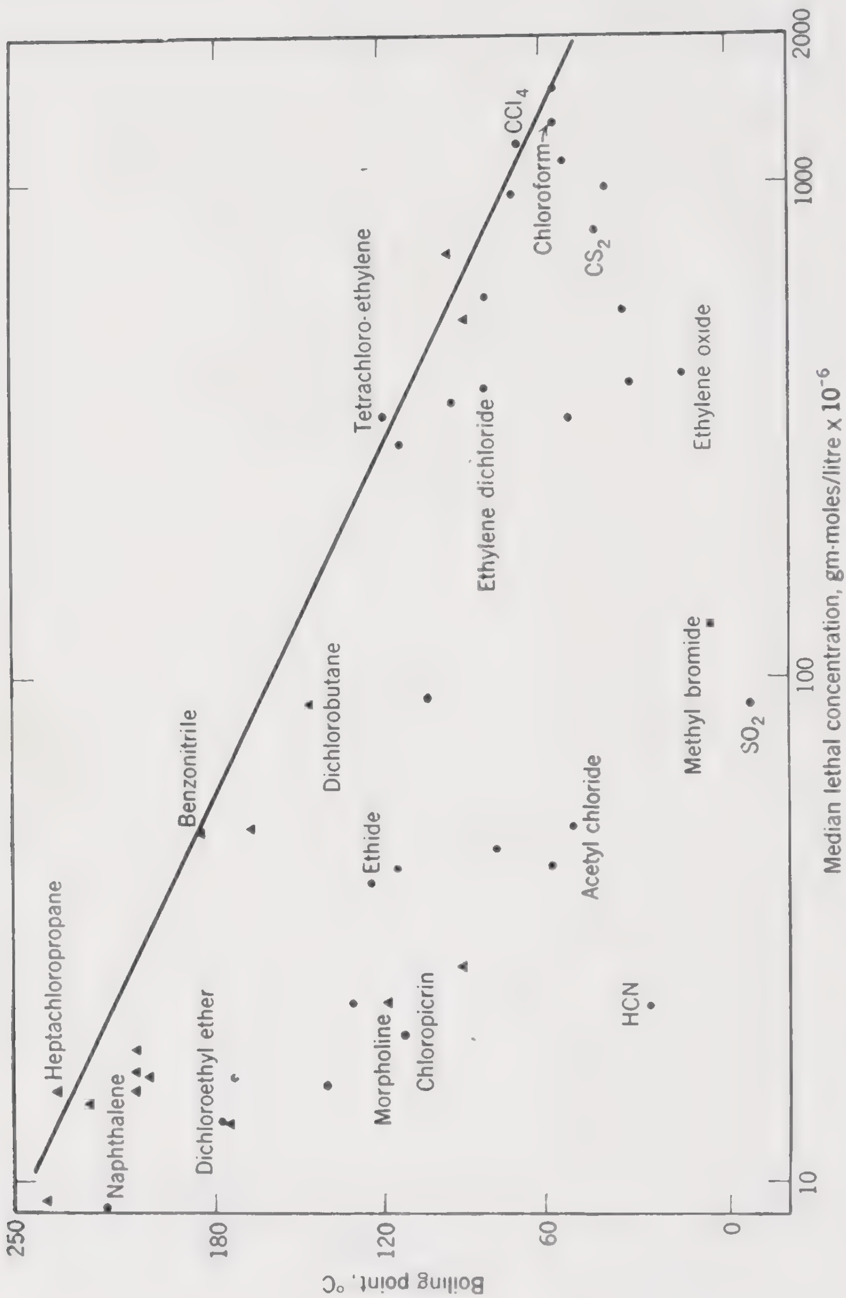


FIG. 6. Relation of toxicity to boiling point of a number of compounds, including unusually powerful fumigants (chemical poisons) as well as physical poisons. (▲ Data of Brown; ● data of Shepard, Lindgren, and Thomas; on *Tribolium*.)

that they act as narcotics or physical poisons which kill when their partition from air to the insect body reaches a level that is physically toxic.[41a]

On the other hand there are volatile compounds which are chemical poisons, which can kill by entering the biochemistry of the body, and which are therefore toxic at very much lower relative saturations. It will be noted in Fig. 6 that a number of compounds show a fumigant toxicity much higher than would be expected from their low boiling point and high volatility. Such compounds include chloropicrin, HCN, SO_2, CS_2, CH_3Br, and nearly all the effective commercial fumigants. Methyl bromide, for example, can kill *Sitophilus* at a thermodynamic activity of 0.004, equivalent to a relative saturation of 0.4%.[41a] It is considered that this enhanced toxicity is due not only to increased adsorption, but also to specific biological reaction. Hydrogen cyanide, SO_2, and CS_2 are highly water-soluble and are readily absorbed into the insect's body. The first two gases are exhaled on return to fresh air, whereas CS_2 is held in the tissues.[156] Chloropicrin, allyl isothiocyanate, and benzyl chloride are known as irritants or lachrymators to man, having the capacity of releasing acid on entering living tissues.

Halogenated aliphatic hydrocarbons

The substitution of halogen atoms in the lower aliphatic hydrocarbons yields an effective group of insect fumigants, of which methyl bromide, ethylene dichloride, and D-D mixture are examples. Of 309 organic vapours tested for toxicity, 15 out of the 18 best compounds contained chlorine. In these volatile fumigants the bromine analogue is probably no less, if not more, toxic than the corresponding chlorinated compound. Bromoform is moderately toxic to *Aonidiella*, chloroform only slightly toxic.[29] In the monohalogenated methanes the toxicity rises chloro < bromo < iodo-methane, along with the boiling point. With heat-generated aerosols of these alkyl halides, only iodoform is toxic to *Musca* adults; bromoform gives a complete but temporary knockdown, but chloroform neither stupefies nor kills.[illegible] Ethylene dibromide is a slightly better fumigant for *Tribolium* than ethylene dichloride (Table 3).

It will be found that there is a tendency for the toxicity of halogenated aliphatics, in common with most fumigants, to rise as the compounds increase in molecular weight. This may be observed in Table 3, which lists the LC_{50} values for adults of *Tribolium confusum*, determined by enclosure in a vessel for 5 hr at 25° C.

TABLE 3. FUMIGANT TOXICITY OF HALOGENATED ALIPHATIC HYDROCARBONS TO *Tribolium confusum*

Compound	Formula	LC_{50}, mg/litre
Hexachloropropene	$CCl_2{=}CCl{-}CCl_3$	1.1
s-Heptachloropropane	$CCl_3{-}CHCl{-}CCl_3$	2.5
2,3-Dichloropropene-1	$CH_2{=}CCl{-}CH_2Cl$	2.9
Hexachlorobutadiene	$CCl_2{=}CCl{-}CCl{=}CCl_2$	4.0
as-Heptachloropropane	$CCl_3{-}CCl_2{-}CHCl_2$	4.1
1,3-Dichloropropane	$CHCl{=}CH{-}CH_2Cl$	10
1,4-Dichlorobutane	$CH_2Cl{-}CH_2{-}CH_2{-}CH_2Cl$	11
Isocrotyl chloride	$CH_2{=}C(CH_3){-}CH_2Cl$	12
Ethylene dichloride [82]	$CH_2Cl{-}CH_2Cl$	19
Propylene dichloride [159]	$CH_2Cl{-}CHCl{-}CH_3$	40
1,1,1-Trichloroethane	$CCl_3{-}CH_3$	66
Dichloromethane	CH_2Cl_2	82
Trichloroethylene [159]	$CCl_2{=}CHCl$	108
Chloroform [82]	$CHCl_3$	157
Carbon tetrachloride [159]	CCl_4	185
Allyl bromide [204]	$CH_2{=}CH{-}CH_2Br$	9
Methyl bromide [159]	CH_3Br	11
Isocrotyl bromide [148]	$CH_2{=}C(CH_3){-}CH_2Br$	14
Ethylene dibromide [204]	$CH_2Br{-}CH_2Br$	14
Butyl bromide [204]	$CH_3{-}CH_2{-}CH_2{-}CH_2Br$	100
Ethyl bromide [148]	$CH_3{-}CH_2Br$	150

Compounds, if not marked by reference number, tested by Brown.[9]
Results of Young and Cotton calculated for 5-hr exposure.[204]

The relationship of toxicity to the boiling points of the chlorinated compounds is shown graphically in Fig. 7. With the exception of trichloroethylene, there is a tendency for the unsaturated compounds to show considerably higher toxicity than their saturated analogues. Both of the alkyl dichlorides, 2,3-dichloropropene-1 and 1,3-dichloropropene (the principal constituent of D-D mixture), are considerably more toxic than propylene dichloride. Of the bromine compounds the unsaturated allyl bromide is outstanding. In soil applications against *Limonius*

it proved to be more toxic than allyl iodide, which in turn was superior to allyl chloride.[93]

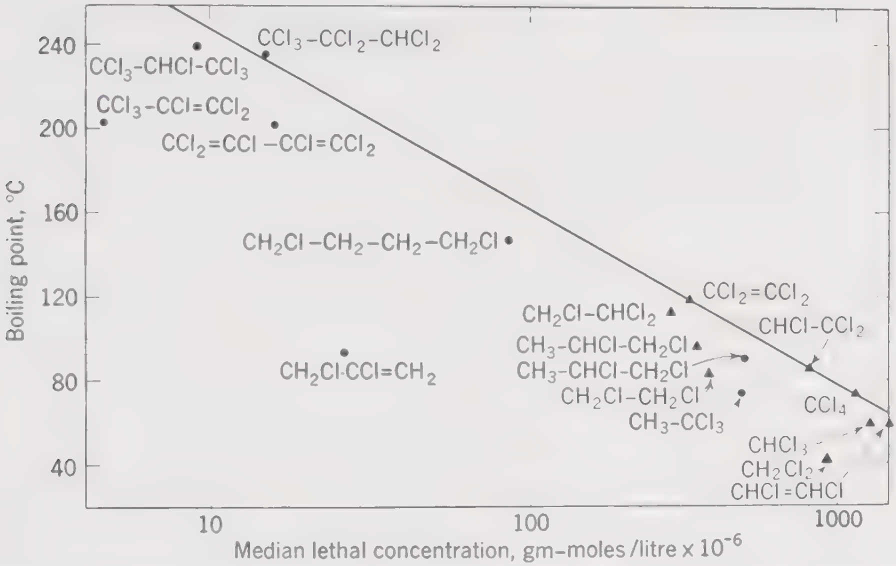


FIG. 7. Relation of toxicity to boiling point of chlorinated aliphatic hydrocarbons. (● Data of Brown; ▲ data of Shepard, Lindgren, and Thomas; on *Tribolium*.)

There would appear to be no regular relationship between toxicity and degree of halogenation. In the chloromethane series, toxicity falls $CH_2Cl_2 > CHCl_3 > CCl_4$ with increasing halogenation (see Table 3). On the other hand, in the ethylene series, toxicity rises *s*-dichloro < trichloro < tetrachloroethylene with increasing halogenation. In the saturated ethane series, *s*-tetrachlorethane is more toxic (to *Cimex*) than ethylene dichloride; whereas trichloromethane is not (to *Tribolium*); both hexachloro- and pentachloroethane show toxicity in aerosols to *Musca*, whereas *s*-tetrachloroethane and ethylene dichloride do not; and ethylene dibromide is very much more toxic than ethyl bromide.[114]

The relative toxicity of halogenated aliphatic hydrocarbons is better understood by comparing the thermodynamic activities, or relative saturations, required to kill; this eliminates the factor of volatility, which varies with boiling point and has nothing to do with toxicity. A full series of determinations have been made on adult *Sitophilus granarius*.[114] For the di- and tri-halogenated methanes, this figure has been determined to be approximately

0.2, and for carbon tetrachloride 0.3, indicating that the median lethal concentrations occurred, respectively, at 20 and 30% relative saturation. For the chlorinated ethanes and ethylenes, and for dichloropropane, the figure lies between 0.24 and 0.37. These compounds may therefore be classed as physical poisons, killing by narcosis rather than biochemical reaction.

TABLE 4. TOXIC THERMODYNAMIC ACTIVITIES OF ALKYL HALIDES FOR *Sitophilus granarius* [41a]

	Chloride	Bromide	Iodide
Methyl	0.014	0.0004	0.0007
Ethyl	0.28	0.075	0.010
Propyl	0.30	0.15	0.014
Isopropyl	0.33	0.37	0.11
Butyl	0.38	0.22	0.036
Amyl	0.40	0.32	0.10

The thermodynamic activities producing a toxicity equivalent to 50% kill are shown for the alkyl halides in Table 4. It may be seen that the methyl halide is sharply the most toxic of each series, and that the order of toxicity is iodides > bromides > chlorides. These results closely parallel the reactivities, as established by velocity constants, of these compounds in organic chemical reactions. The figures show that a high proportion of the lower alkyl bromides and iodides may be classed as chemical poisons.[41a]

Alkyl nitro compounds

Nitration of the lower paraffins results in the production of nitroalkanes, which are effective fumigants. The toxicity rises with molecular weight from nitromethane through nitroethane and nitropropane to 1-nitrobutane, which shows an LC_{95} for *Tribolium* of 10 mg litre [149] (Table 5). Substitution in the 2 position instead of the 1 reduces the toxicity of nitrobutane and nitropropane by one-half.

Halogenation of the nitroalkanes produces a further and considerable increase of fumigant toxicity. Whereas at a concentration of 20 mg litre nitroethane causes no mortality of *Aonidiella*, either 1-chloro- or 1,1-dichloronitroethane will induce 100% kill. Similarly 1-chloro-1-nitropropane at 20 mg litre kills all these

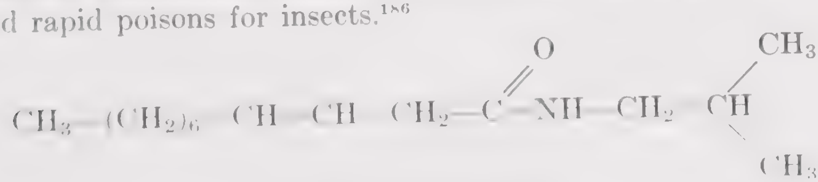
scale insects, whereas 1-nitropropane at this concentration kills none.[29] The chlorinated nitromethane, chloropicrin (CCl_3NO_2), is one of the most toxic fumigants now in general use. In tests with *Cimex*, 1,1-dichloro-1-nitroethane has proved to be 4 times as powerful as nitroethane and approached chloropicrin in toxicity.[147] This material, marketed under the name *Ethide*, is also more toxic than nitroethane to *Tribolium*. It was noted that whereas chloropicrin was moderately toxic to *Aonidiella*, bromopicrin was only slightly so.[29]

TABLE 5. FUMIGANT TOXICITY OF NITROALKANES TO *Tribolium* AND *Cimex*

Compound	Formula	LC_{95}, mg/litre *Tribolium*[149]	LC_{95}, mg/litre *Cimex*[147]
Nitroethane	$CH_3—CH_2—NO_2$	14	32
1-Nitropropane	$CH_3—CH_2—CH_2—NO_2$	16	20
1-Nitrobutane	$CH_3—CH_2—CH_2—CH_2—NO_2$	10	32
Chloropicrin	$CCl_3—NO_2$	4[159]	5
1,1-Dichloro-1-nitroethane	$CH_3—CCl_2—NO_2$	12	8
1,1-Dichloro-1-nitropropane	$CH_3—CH_2—CCl_2—NO_2$	11[148]	..

Aliphatic amines and amides

The lower members of the alkyl amine series are volatile. Their fumigant toxicity, as determined on *Sitophilus*, equals or surpasses that of CS_2 or better. The peak in the series is reached with *n*-propylamine ($C_3H_7NH_2$) with an m.l.c. of 8 mg/litre, which, however, is only one-half as toxic as ammonia.[11a] The higher members show a measure of contact toxicity, reaching a maximum at di-*n*-octylamine for *Musca* larvae.[72] Triamylamine has been found to be highly toxic to *Pediculus*, along with the 2,2-diethoxy derivatives of diamylamine, di(3-methylamyl)-amine and di(2-butylhexyl)amine.[10] Of the quaternary ammonium compounds, tetramethylammonium salts are effective and rapid poisons for insects.[186]



N-Isobutylundecylenamide

The unsubstituted aliphatic amides show negligible toxicity over the full ascent of the series to palmitamide. However, alkyl substitution on the amide nitrogen yields some good lousicides, such as N,N-diamyl- and diisoamyl-acetamide, and diethylundecylenamide. N-Isobutylundecylenamide is an excellent synergist for pyrethrins. Even better for promoting knockdown and kill of houseflies and mosquitoes was N,N-dipropyl-3-hydroxy-3-methylvaleramide. Another effective substituted amide in this regard was N,N-dipropylsuccinamic acid, whose allyl ester was highly effective as a synergist.[94]

Alkyl nitriles

The first of the series, hydrogen cyanide, which may be regarded as the nitrile of formic acid, is one of the most toxic fumigants for insects, as for most forms of life. The m.l.c. of this gas for *Tribolium* has been determined to be 0.6 mg litre. The lower alkyl cyanides are non-toxic to *Aonidiella*, the scale insect which has shown resistance even to hydrogen cyanide.[29] On the other hand, both butyronitrile and valeronitrile have proved to be highly toxic fumigants for *Sitophilus oryzae*.[152] The higher nitriles from octanoyl- to octadecanoyl-nitrile have no fumigant toxicity although they are slightly volatile. They show repellency without toxicity to caterpillars.[106] They proved to be moderately toxic to *Musca* and *Ephestia* larvae,[11] and tridecanoylnitrile (lauryl cyanide, $C_{12}H_{25}CN$) has been used in fly sprays.[11]

Hydrogen cyanide	$H—C{\equiv}N$
Butyronitrile	$CH_3—CH_2—CH_2—C{\equiv}N$
Acrylonitrile	$CH_2{=}CH—C{\equiv}N$
Cyanogen chloride	$Cl—C{\equiv}N$
Chloroacetonitrile	$Cl—CH_2—C{\equiv}N$
Trichloroacetonitrile	$Cl_3—C—C{\equiv}N$

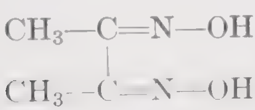
Acrylonitrile, in which the alkyl chain is unsaturated, is one of the best fumigants available.[118] Of the higher analogues, alkyl-substituted hexenenitriles are effective poisons for lice.[illegible]

Halogenation improves the fumigant toxicity of nitriles. Cyanogen chloride is as toxic as HCN [127] but is also dangerous to use. The next analogue, chloroacetonitrile, is an excellent fumigant, surpassing its di- and trichloro derivatives.[117] The m.l.c. of chloroacetonitrile and acrylonitrile to *Tribolium* is less than 2 mg litre.[118] The chlorination of acrylonitrile, however, does not increase its fumigant toxicity.[26]

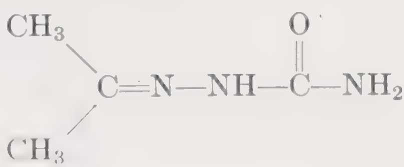
Other nitrogenous aliphatics

Urea and its alkyl and acyl derivatives have shown no more than negligible toxicity to insects, with the exception of the moderately insecticidal 1-*tert*-amyl-urea.[181] Of the allophanates, the isopropyl ester is the most toxic, but it affords only slight to moderate protection against codling moth.[168] Tests on leaf-eating insects revealed that neither nitro- nor cyano-guanidine was toxic,[184] but guanidine carbonate afforded partial protection against *Carpocapsa*, and guanidine thiocyanate was very toxic to this species.[108]

All the aliphatic monoximes tested were non-toxic to phytophagous insects. However, dimethyl glyoxime, a dioxime, showed moderate toxicity to *Bombyx* larvae.



Dimethyl glyoxime

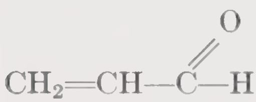


Acetone semicarbazone

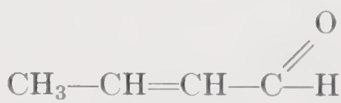
The aliphatic semicarbazones as a class are highly insecticidal. When tested as contact dusts on leaf-feeding insects, acetone and butanone semicarbazones proved to be good insecticides, whereas the semicarbazones of 2-pentanone, heptanone, and octanone were ineffective.[185] However, when applied to apple plugs as protection against *Carpocapsa*, the semicarbazones of 2-heptanone and octanone were more effective than those of butanone and pentanone.[166, 180] The aliphatic 2-pentanone semicarbazone was only half as effective as the cyclopentanone semicarbazone. The symmetrical 2,4-dimethyl-3-pentanone semicarbazone is highly insecticidal.

Aldehydes and ketones

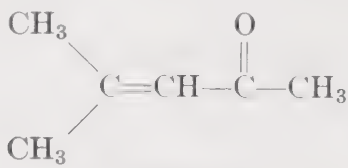
Formaldehyde, the first in the series, has been effectively employed as a stomach poison for houseflies and maggots and as a mothproofing agent,[14] although it has little value as a fumigant. Its homologues from acetaldehyde to valeraldehyde show no fumigant toxicity to *Aonidiella;*[29] but they are moderately poisonous to *Sitophilus*, to which enanthaldehyde (C_7) is highly toxic. The unsaturated aldehydes such as acrolein (acrylaldehyde), crotonaldehyde, and α-methyl-β-ethylacrolein are all powerful fumigants for *Sitophilus*. It will be noted that these unsaturated aldehydes show the toxic C=C—C=O configuration.



Acrolein



Crotonaldehyde



Mesityl oxide

The first member of the ketone series, acetone, is slightly toxic to insects on injection and on contact. None of the ketones whose vapours were tested in the series from acetone to 2-hexanone and diisopropyl ketone showed an effect on *Aonidiella*,[29] but all those tested up to butyrone (dipropyl ketone) were toxic to *Sitophilus*.[152] 2-Tridecanone (methyl undecyl ketone) proved to be an effective stomach poison for *Bombyx* larvae.[53] The most insecticidal of the ketones is the unsaturated mesityl oxide, which shows high toxicity to both *Sitophilus* and *Carpocapsa;* its molecule contains the C=C—C=O grouping.

Ethers

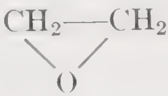
The more volatile aliphatic ethers are narcotic to insects, as to higher animals. Propyl ether was found to be moderately toxic, and isopropyl ether highly toxic, to *Aonidiella*.[29] Of the chlorinated ethers, dichloromethyl ether proved to be a powerful fumigant for *Sitophilus*,[152] although without action on *Aonidiella*.

The β,β′-dichloroethyl ether is a highly effective fumigant for wireworms and other soil insects, whereas the α,β isomer is virtually non-toxic.[93]

Primary alcohols of the aliphatic series which contain ether linkages show considerable contact toxicity. Both butyl cellosolve ($C_4H_9—O—C_2H_4OH$) and butyl carbitol ($C_4H_9—O—C_2H_4—O—C_2H_4OH$) are highly poisonous to *Lucilia* larvae. The latter compound, with its toxicity further increased by substitution of SCN for the alcoholic OH, becomes the active principle of the insecticide *Lethane 384*.[95]

$Cl—CH_2—CH_2—O—CH_2—CH_2—Cl$

β,β′-Dichloroethyl ether



Ethylene oxide

Ethylene oxide is a fumigant of considerable value, having proved effective against *Tribolium* and highly effective against *Aonidiella*. Substitution of a chloromethyl group on the ring yields epichlorohydrin, which has shown high toxicity to *Lucilia* and *Limonius*. Substitution of chlorine by opening the —O— linkage in the ring gives ethylene chlorohydrin ($CH_2OH—CH_2Cl$), which is four times as effective as epichlorohydrin to *Limonius*.[92]

Treatment of ethylene oxide with hydrofluoric acid results in ethylene fluorohydrin or fluoroethyl alcohol ($FCH_2—CH_2OH$); it is the parent compounds of a class of fluoro ethers which are generically termed "fluorohydrins," but are really methylals of fluoroethyl alcohol.[105] They are highly toxic to insects and exhibit the property of being translocated in plants to make the tissues insecticidal; they have thus been classed as systemic insecticides. The first to be discovered was di(β-fluoroethoxy)-methane ($F—C_2H_4—O—CH_2—C_2H_4—F$), but it was too highly toxic to mammals. The β-fluoroethyl monether of glycol ($F—C_2H_4—O—C_2H_4OH_2$) was less toxic to mammals while still being highly insecticidal. The most powerful of the fluorohydrin systemic insecticides is di(fluoroethoxyethoxy)methane, which

$F—CH_2—CH_2—O—CH_2—CH_2—O—CH_2—O—CH_2—CH_2—O—CH_2—CH_2—F$

Di(fluoroethoxyethoxy)methane

can kill caterpillars as well as aphids feeding on the treated plants.[105] It is interesting to observe that the fluorine compound, sodium fluoroacetate (the rodenticide *1080*), has proved to be a powerful systemic poison for aphids on broad beans.[31a]

Esters

The simpler and more volatile esters are powerful fumigants. For example, both methyl acetate and methyl propionate are highly toxic to *Aonidiella*.[29] There is evidence that in certain cases the fumigant toxicity of esters is decided more by the nature of the acyl radical than the alkyl radical. The formates are more toxic than their corresponding acetates to *Sitophilus* (Table 6). The methyl and ethyl formates both showed the same m.l.c. to *Tribolium*, which was one-quarter the m.l.c. of 80–90 mg/litre established for the methyl and ethyl acetates.[41a] The methyl, propyl, and butyl esters of butryic acid all manifested the same order of toxicity to *Limonius*.

TABLE 6. Fumigant Toxicity of Aliphatic Esters to *Sitophilus granarius* [41a]

Median lethal concentrations, mg/litre

Alkyl Ester	Formate	Acetate
Methyl	15	84
Ethyl	35	56
Propyl	28	45
Isopropyl	34	90

However, with the formates that were tested against *Limonius*, there was a great difference in toxicity between the methyl ester, which was the best, and the octyl ester, which was the least effective of the series. Against *Sitophilus*, methyl formate was the outstanding ester.[41a] And in tests with propionates against *Aonidiella*, the methyl ester was decidedly toxic, the propyl moderately, and the ethyl only slightly effective. The relation of toxicity to the acyl group concerned showed no uniformity, for although the formate (methyl ester) was more toxic than the acetate against *Tribolium* or *Sitophilus*, it was found to be considerably less toxic than the acetate or propionate against *Aonidiella*.

$$CH_2{=}CH{-}\overset{\displaystyle O}{\overset{\|}{C}}{-}O{-}CH_2{-}CH_3$$

Ethyl acrylate

$$CH_2{=}CH{-}CH_2{-}O{-}\overset{\displaystyle O}{\overset{\|}{C}}H$$

Allyl formate

The unsaturated allyl group is the most toxic alkyl substituent. Of all the esters tested against *Limonius*, allyl formate was best, being surpassed only by allyl halides.[93] Similarly, the unsaturated acrylic radical is the most toxic acyl substituent; of all the esters tested against *Aonidiella* ethyl acrylate was best.[29] Both of these esters have irritant vapours and are stimulating to the insects, and both contain the $C{=}C{-}C{=}O$ grouping.

Esters of the dibasic carbonic acid show fumigant activity; both the dimethyl and diethyl carbonates are definitely toxic to *Sitophilus*.[152] Addition of halogen to the slightly toxic monomethyl carbonate improves the effectiveness, for methyl chlorocarbonate is moderately toxic to *Aonidiella;* no such improvement eventuates with ethyl chlorocarbonate.[29] Propyl chlorocarbonate is highly toxic to *Aonidiella*. The chloroacetate of butyl carbitol is considerably more effective than the acetate, surpassing even the thiocyanate (*Lethane 384*) in toxicity but not in speed of action.[95]

The diesters of dibasic fatty acids are quite powerful insect poisons. The diethyl and dibutyl oxalates have been found to be effective against *Carpocapsa*. The diethyl ester of maleic acid is toxic to *Musca*, and of malonic acid to *Leptinotarsa* and *Tinea*. The esters of malic and adipic acids are effective as area sprays against chiggers. The unsaturated diallyl ester of adipic acid is highly toxic as a fly spray.[44] Both diallyl succinate and adipate are excellent louse ovicides, while the diallyl ester of the unsaturated fumaric acid is even better.[41]

Mercaptans, sulphides, and disulphides

The mercaptans or alkanethiols ($R{-}SH$) are effective insect fumigants. Both ethyl and *n*-butyl mercaptan are highly toxic to *Sitophilus*. Only isobutyl mercaptan proved to be a good fumigant for *Aonidiella*. The most effective of the series against *Limonius* was found to be *n*-propyl mercaptan, but its toxicity was only moderate. Perchloromethyl mercaptan was one of the

best auxiliary gases (irritants) for hydrogen cyanide fumigation.[138]

The toxicity of the sulphides is slight, although diethyl sulphide is moderately effective against *Aonidiella*. The disulphides (R—S—S—R) are also mediocre in performance with the exception of methyl disulphide, which is highly effective against *Limonius* and *Sitophilus*. The higher members of the sulphide and disulphide series show equally slight toxicity to *Lucilia* larvae.

Thiocyanates and isothiocyanates

The lower alkyl thiocyanates (R—S—C≡N) are excellent fumigants, approaching HCN in toxicity, but unfortunately their vapours are phytotoxic. The methyl and ethyl thiocyanates are the most effective, being highly toxic to *Aonidiella*, *Sitophilus oryzae*, and *S. granarius*.[128] High contact toxicity was shown to *Pediculus* by *n*-octyl thiocyanate,[40] but 2-octyl thiocyanate was inferior in sprays against *Aphis*.[67] Contact toxicity rises as the series approaches lauryl thiocyanate, an insecticide with excellent knockdown properties. Against *Cimex*, the m.l.c. of octyl, decyl, or lauryl (C_{12}) thiocyanate was determined to be 5%, indicating that the toxicity on a molar basis is at a peak with lauryl thiocyanate. Beyond lauryl thiocyanate, toxicity falls again as the m.l.c. increases to 11% for myristyl (C_{14}), 18% for cetyl (C_{16}), and 25% concentration for stearyl (C_{18}) thiocyanate.[20] Lauryl thiocyanate was found to be equitoxic with capric and myristic thiocyanates for aphids, but superior to either for red spider, for which it is also an effective ovicide.[105] The unsaturated allyl thiocyanate has been found to be toxic to the potato beetle.[44]

The isothiocyanates are structural isomers of the thiocyanates in which alkyl substitution occurs on the nitrogen instead of the sulphur. Both methyl and ethyl isothiocyanates (R—N=C=S) proved to be highly toxic to *Aonidiella*. Ethyl isothiocyanate was found to be an excellent soil fumigant for *Limonius*, being some 100 times more effective than ethyl thiocyanate. Allyl isothiocyanate was even more poisonous to *Limonius*, and it has

shown outstanding toxicity as a fumigant for *Aonidiella*,[20] *Musca*,[120] *Agriotes*,[190] *Sitophilus* (two spp.), and *Tribolium*.[128]

$$C_4H_9{-}O{-}C_2H_4{-}O{-}C_2H_4{-}S{-}C{\equiv}N$$

β-Butoxy-β′-thiocyanodiethyl ether (in *Lethane 384*)

$$N{\equiv}C{-}S{-}CH_2{-}CH_2{-}O{-}CH_2{-}CH_2{-}S{-}C{\equiv}N$$

β,β′-Dithiocyanodiethyl ether (in *Lethane B-71*)

$$C_{11}H_{23}{-}\overset{\overset{\large O}{\|}}{C}{-}O{-}C_2H_4{-}S{-}C{\equiv}N$$

Thiocyanoethyl laurate (in *Lethane 60*)

$$C_4H_9{-}O{-}C_2H_4{-}O{-}C_2H_4{-}O{-}\overset{\overset{\large O}{\|}}{C}{-}CH_2{-}S{-}C{\equiv}N$$

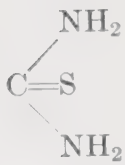
Butylcarbitol β-thiocyanoacetate (in *Lethane 440*)

The commercial thiocyanates known as *Lethanes* were originally alkyl thiocyanates.[125] More recent *Lethanes* are derived from thiocyanation of the alkyl groups of ethers, or of the alkyl or acyl groups of esters.[67] These compounds cause quick knockdown and have been developed as contact insecticides. It has been shown that whereas the alkyl thiocyanates have poor knockdown value, the alkyl thiocyanoacetates show rapid knockdown, and the α-thiocyanoketones even more so, reaching a maximum at about C_6.[59]

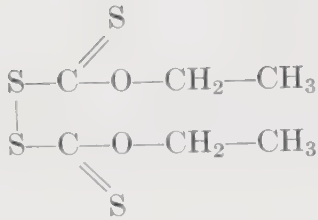
Thiourea, thiocarbamates, and thiuram compounds

Thiourea is highly toxic to larvae of *Musca*,[110] *Drosophila*,[57] *Lucilia*,[72] and *Tineola*.[119] However its value as a poison for mosquito larvae or leaf-feeding insects is slight.[22] None of its alkyl derivatives, including the N-allyl, proved to be as toxic as thiourea itself.[72, 180]

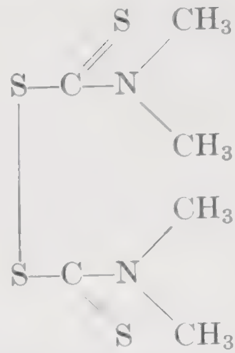
The thioamides are more toxic than the corresponding oxygenated amides. The N-allyl derivatives of thioacetamide ($CH_3{-}CS{-}NH_2$) and thiopropionamide approach thiourea in toxicity.[72] Another C=S compound is bis-ethyl xanthogen, which has been developed as a lousicide in Russia; tests have shown it to be superior to *Lethane 60* but inferior to *Lethane 384* or lauryl thiocyanate.[20]



Thiourea



Bis-ethyl xanthogen



Tetramethyl thiuram disulfide

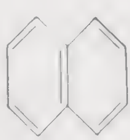
The alkyl derivatives of dithiocarbamic acid are toxic to aphids and mites. They are also effective against the phytophagous beetles *Epilachna* and *Popillia*, because they inhibit feeding.[192] The S-ferric salt of dimethyl-dithiocarbamate provides highly effective protection against these beetles. The hexahydrate of disodium ethylene bisdithiocarbamate has been found to give excellent control of the pear psylla.[23]

The fungicide tetramethyl thiuram disulphide (TMTD) has also been found to give effective control of *Popillia*, *Epilachna*, and *Leptinotarsa*.[60,195] Against *Bombyx*[54] or *Prodenia* larvae[184] it is, however, non-toxic. The effectiveness of this symmetrical molecule as a fungicide has been correlated with the presence of the C=S group rather than the S—S linkage.[71] Other thiuram disulphides proved to show negligible toxicity to these beetles. Tetramethyl thiuram sulphide is highly toxic to *Epilachna* and *Leptinotarsa* but not to *Popillia*.[192]

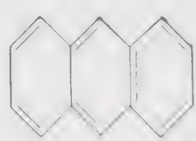
Cyclic hydrocarbons

Neither benzene nor cyclohexane shows contact or stomach toxicity to insects.[15,143] Addition of methyl groups increases contact toxicity in the series benzene < toluene < xylene. Further methylation to produce mesitylene and pseudocumene, pentamethylbenzene, and hexamethylbenzene destroys the insecticidal activity.[15,183]

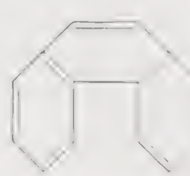
Benzene



Naphthalene



Anthracene



Phenanthrene

Contact toxicity shows a material rise with the double-ringed naphthalene, in which two carbon atoms are shared by two benzene rings. Its hydrogenated derivatives decrease in toxicity in the series naphthalene > tetralin > decalin.[186] The toxicity also falls with the three-ringed compound anthracene, which is inferior to its isomer phenanthrene.[15, 13] Chrysene, with a four-ringed molecule, is quite inactive.[15] Acenaphthene and fluorene, each with one cyclopentene and two benzene rings, are slightly toxic.[180, 183]

Where the two benzene rings are linked from the carbon atom of one to the carbon atom of the other, as in biphenyl, the toxicity to insects is greatly increased. Hydrogenation of one ring, as in phenylcyclohexane, reduces its insecticidal power.[15] Addition of further benzene rings, as in diphenylbenzene and triphenylbenzene, results in complete loss of toxicity.[186]

Derivatives of benzene

Benzene itself is practically non-toxic to insects as a contact or stomach poison. However, the addition of simple groupings or radicals to benzene will produce many effective poisons. Thus an opportunity is presented of evaluating the effect of introducing certain supposed toxophoric groups into the molecule. The principal toxophores are considered to be NO_2, CO, CN, and SCN.

Studies on the contact toxicity of monosubstituted benzene to *Aphis* have shown that introduction of a CH_3 or NH_2 group roughly doubles the toxicity, of a Cl (or other halogen), OH, or OCH_3 group increases it 5–10 times, and introduction of an NO_2 group increases it 100 times (Table 7).

TABLE 7. Contact Toxicity of Substituted Benzenes to *Aphis rumicis*

Compound	Formula	LC_{95}*	LC_{50}†	Dipole Moment[91]
Benzene	C_6H_6	25	Neg.	0.0
Toluene	$C_6H_5—CH_3$	16	25	+0.4
Aniline	$C_6H_5—NH_2$	15	.....	−1.5
Chlorobenzene	$C_6H_5—Cl$	6.0	4.5	−1.6
Phenol	$C_6H_5—OH$	5.5	2.0	−1.7
Anisole	$C_6H_5—OCH_3$	....	5.0	−1.2
Nitrobenzene	$C_6H_5—NO_2$	....	0.25	−4.2

* Concentration of spray for 95% kill[143] and † for 50% kill.[189]

There is a tendency for the more polar compounds, i.e. those with higher dipole moments, to be the more toxic. Polarity is induced by the substituent radical displacing the centre of negative (electron) charges from that of the positive (nuclear) charges in the molecule, resulting in an electrostatic charge which causes it to orient in an electric field; the dipole moment is thus the measure of the electrostatic asymmetry of the molecule.[91] The polar Cl, NH_2, and OH groups confer moderate toxicity, and the highly polar NO_2 group confers high contact toxicity. The great biological activity toxicity of nitrobenzene may be related to the capacity of the highly acidic nitro group to withdraw electrons from the ethylenic double bond in the benzene ring, in the configuration $C{=}C{-}NO_2$.

The classical toxic groupings CO, CN, and SCN also induce high dipole moments when attached to benzene, and so does the COOH group. However, none of these compounds (i.e. benzaldehyde, benzonitrile, phenyl thiocyanate, and benzoic acid, respectively) shows contact toxicity to *Aphis*.[67, 143] But it must be remembered that contact action is a special case requiring the molecule to possess liposolubility in addition to toxicity, in order to penetrate the insect epicuticle. These compounds do show stomach or fumigant toxicity, or are poisonous by injection. Thiophenol (with SH), benzenesulphonic acid (SO_3H), and nitrosobenzene (NO) show only slight insecticidal activity.[15, 43, 72]

Further substitution of additional CH_3 groups increases contact toxicity slightly with the dimethylbenzenes or xylenes,[186] but it disappears with the tri-, penta-, and hexamethylbenzenes.[15, 183] However, the fumigant toxicity increases twice for every step from benzene < toluene < xylene < pseudocumene, a rate consistent with the relation of toxicity to boiling point. Disubstitution with NH_2 groups increases the activity in the case of *p*-phenylenediamine and (probably) *o*-diaminobenzene;[15] *m*-diaminobenzene, however, is non-toxic.[183]

The insecticidal activity of polyphenols decreases with the dihydroxybenzenes (pyrocatechol, resorcinol, and hydroquinone), and still further with the trihydroxybenzene pyrogallol. Multiplication of these polar groups results in an increase of the water/benzene partition coefficient and a decrease in lipoid solubility;[186] the surface activity also decreases.[151] On the other

hand, continuing substitution of OCH_3, the methyl ether group which confers liposolubility, results in an increase of toxicity from anisole to veratrole (1,2-) to trimethoxybenzene (1,2,3-).[186] An increase of nitro groups results in heightened toxicity in the case of *m*- *and* *p*-dinitrobenzene, but not of the *ortho* isomer. However, it does not increase further with trinitrobenzene, although the toxicity of all these compounds is at a high level.[15,186]

The addition of Cl to chlorobenzene has the effect of enhancing its toxicity. The fumigant effectiveness of chlorinated benzenes to *Agriotes* larvae was found to increase 3 times for every chlorine atom added.[190] Both *o*- and *p*-dichlorobenzene (PDB) are quite highly toxic, but *m*-dichlorobenzene is only slightly so. The most toxic of the series is 1,2,4-trichlorobenzene, after which there is a decrease to 1,2,4,5-tetrachloro- and hexachlorobenzene.[186] Replacement of chlorine by another halogen (fluorine, bromine, or iodine) does not increase the effectiveness;[190] the dibromobenzenes are toxic but the diiodobenzenes are not. Where the effect of mixed halogenation of benzene has been tested, *p*-chloroiodo- and *p*-bromoiodo-benzene have proved to be good insecticides for caterpillars,[183] but *p*-chlorobromobenzene is not even appreciably toxic.[106]

TABLE 8. INSECTICIDAL ACTIVITY OF DISUBSTITUTED BENZENES

- - Inactive. — Slightly toxic. = Moderately toxic. ≡ Highly toxic.

Data from many authors.

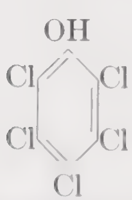
	H	Cl	NO_2	OH	NH_2	CH_3
H	- -	—	=	—	- -	- -
Cl	—	$\underset{=}{o}$, $\underset{=}{p}$	$\underset{\equiv}{o}$, $\underset{\equiv}{m}$, $\underset{\equiv}{p}$	$\underset{-}{p}$	$\underset{-}{o}$, $\underset{-}{p}$	$\underset{--}{o}$, m, p
NO_2	=	$\underset{=}{o}$, $\underset{\equiv}{m}$, $\underset{\equiv}{p}$	$\underset{\equiv}{m}$, $\underset{\equiv}{p}$	$\underset{=}{p}$ *	$\underset{=}{o}$	$\underset{=}{p}$
OH	—	$\underset{-}{p}$	$\underset{=}{p}$	$\underset{-}{o}$	$\underset{-}{p}$	$\underset{-}{o}$, $\underset{-}{m}$, $\underset{-}{p}$
NH_2	- -	$\underset{-}{o}$, $\underset{-}{p}$	$\underset{=}{o}$	$\underset{-}{p}$	$\underset{-}{p}$	$\underset{-}{o}$
CH_3	- -	$\underset{--}{o}$, $\underset{--}{m}$, $\underset{--}{p}$	$\underset{=}{p}$	$\underset{-}{o}$, $\underset{-}{m}$, $\underset{-}{p}$	$\underset{-}{o}$	$\underset{--}{o}$, $\underset{--}{m}$, $\underset{--}{p}$

* For example, *p*-nitrophenol, the best of the nitrophenols, is moderately toxic.

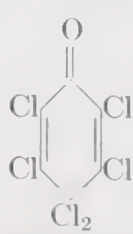
The effect of disubstituting benzene with one each of the different substituents is shown in Table 8. In this table the toxicity of the most active isomer or isomers of each disubstituted compound is indicated by the number of underlines. It will be found that the toxicity of the resulting compound is in no case greater than that of a benzene disubstituted with the better substituent. Addition of a nitro group has an activating effect on all the monosubstituted benzenes. Only the chloro and nitro groups have the capacity to increase the toxicity of nitrobenzene.

Of the three possible arrangements of the two substituents on the benzene ring, the *para* position is most frequently the best for insecticidal effect, followed by the *ortho* position, which is sometimes better. The *meta*-substituted benzene is never the most toxic isomer, and only in the case of the substituted toluenes and the dinitro- and chloronitrobenzenes does it show a toxicity comparable to the other structural isomers. When identical groups (or groups with similar polarity) are substituted in the *para* position, the dipole moment is nearly zero[91] and the total surface energy is at a minimum.[65] The *meta* compounds are stated to have the highest molecular surface energies of the three isomers.[65]

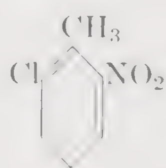
The chlorination of dinitro- or trinitrobenzene results in no increase or a slight decrease in toxicity.[186] Halogenation of phenols does not enhance insecticidal activity, except in the case of pentachlorophenol and hexachlorophenol, which are highly toxic to caterpillars and lice[10,168,183] and have been developed commercially as insecticides. Chlorination of 2,6-dinitrophenol in the 4 position gives an excellent poison, but it is scarcely better than the parent compound. The 2,6-dichloro and -dibromo derivatives of 4-nitrophenol are considerably toxic, but again they are no better contact insecticides than the parent compound.[15,186]



Pentachlorophenol



Hexachlorophenol (*Keto form*)



6-Chloro-2-nitrotoluene

The halogenation of anilines does not usually increase their toxicity. However, *o*-iodoaniline and 2,5-dichloroaniline were found to be very effective against caterpillars,[183] and the latter compound is also a lousicide.[40] Halogenation of the methylanilines (toluidines) does not induce toxicity except in the case of 4-bromo-*o*-toluidine.[182] It will be noted that in the toxic anilines the position of the substituent is *ortho* to the amino group. Halogenation of the amino nitrogen of aniline produces the toxic hydrochloride and hydrobromide.[181]

None of the substituted benzenesulphonic acids and thiophenols show any increase in toxicity over the almost ineffective parent compounds. Of the substituted benzaldehydes, only mesitaldehyde (3,5-dimethyl) is poisonous to any extent.[40] Of the derivatives of benzoic acid, the only compounds with significant activity are 3,5-diiodo- and 3,5-dinitro-salicylic acid (I_2-ϕ-OH-COOH).[15,183]

The toxicity of toluene is not enhanced by chlorination, but the nitrotoluenes do profit from addition of chlorine. For example, 4-chloronitrotoluene is a good insecticide, and 2-chloro-6-nitrotoluene is excellent.[40,178] The substitution of Cl or OH in *m*-xylene yields moderately toxic compounds, such as 2,6-xylenol, ϕ-$(CH_3)_2$-OH.[40,183]

Nitration of nitrophenol results in the highly toxic dinitrophenols, of which the 2,4 isomer is best, and the 2,5 isomer (the most water-soluble) is least toxic. Further nitration yields the highly water-soluble picric acid (2,4,6-trinitrophenol) and results in a decrease of toxicity. Nitration of anisole yields the significantly insecticidal *o*- and *p*-nitroanisole, but 2,4-dinitroanisole and trinitroanisole are less active.[186]

If the three cresols (which show equal contact toxicity) are nitrated, it will be found that 5-nitro-*o*-cresol is the most toxic of the nitrocresols, followed by 2-nitro-*m*-, 3-nitro-*p*-, 4-nitro-*m*-, and 3-nitro-*o*-cresol (Table 9). Both 2,4-dinitrophenol (DNP), the most toxic of the dinitrophenols, and 5-nitro-*o*-cresol contain a nitro group in *para* position to the phenolic OH group. If these two molecules are combined to produce 3,5-dinitro-*o*-cresol, the result is an extremely effective contact insecticide.[189] This compound is commercially produced under the initials DNOC; it is generally known as 4,6-dinitro-*o*-cresol by organic chemists.

when the OH group and not the CH_3 is considered to occupy the number 1 position for purposes of nomenclature. Analogues which are used as insecticides and ovicides, where a compromise has been struck between a low phytotoxicity and a high insecticidal power, are 4,6-dinitro-*o-sec*-butylphenol (DNBP) and the crotonate of dinitrocaprylphenol (*Arathane*).

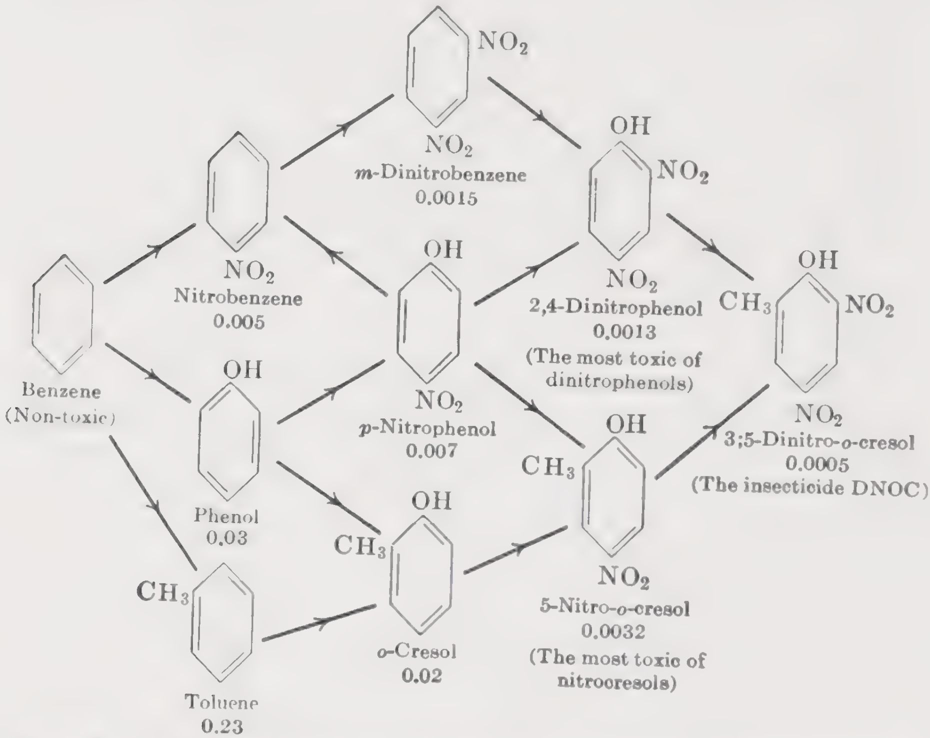


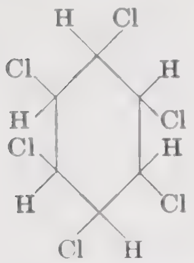
TABLE 9. THE RELATION OF STRUCTURE TO TOXICITY IN NITROPHENOLS AND NITROCRESOLS

The figures represent the concentration of the compound in the spray, in moles per 100 cc. for 95% kill of *Aphis rumicis*. (Data from Tattersfield)

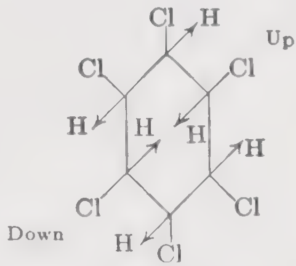
Benzene hexachloride

Chlorination of benzene in the presence of light produces benzene hexachloride ($C_6H_6Cl_6$ or "666"). This is not a benzene derivative such as hexachlorobenzene, but is a saturated naphthenic compound, correctly termed hexachlorocyclohexane, in which the double bonds have become saturated with hydrogen. This material is highly toxic to insects, but the activity varies

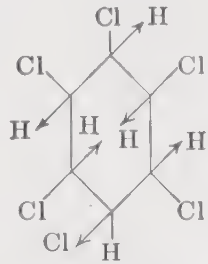
according to the proportion of the different isomers present in the preparation.[171]



Hexachlorocyclohexane

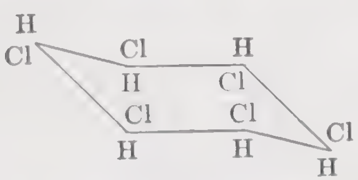


Beta isomer

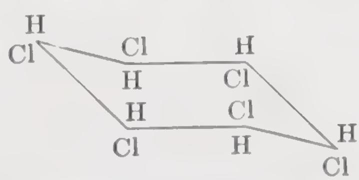


Gamma isomer

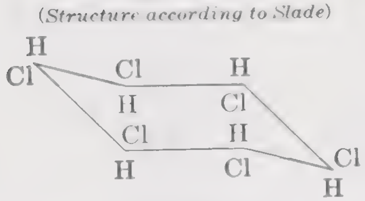
Since there are possibilities of asymmetry in the carbon atoms, dependent upon the disposition of the chlorine and hydrogen substituents, there are stereo-isomers of benzene hexachloride. If the cyclohexane ring lay in one flat plane, substitution could be either upwards or downwards from that plane. But since it is centrosymmetrical and folded, one of the two sets of free valencies point straight outwards from the ring.[171] The folding, in its strainless form, results in a structure which may be regarded as a chair, for which one carbon atom provides the back, another (opposite to it) the foot, and the remaining four the seat.[15] Of the sixteen possible isomers, six are now known.[196]



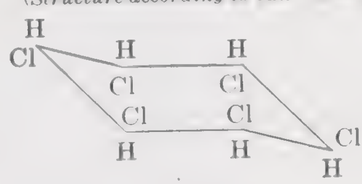
Gamma isomer
(*Structure according to Slade*)



Gamma isomer
(*Structure according to van Vloten*)



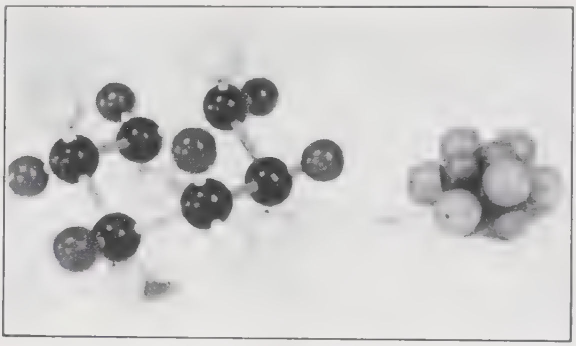
Beta isomer



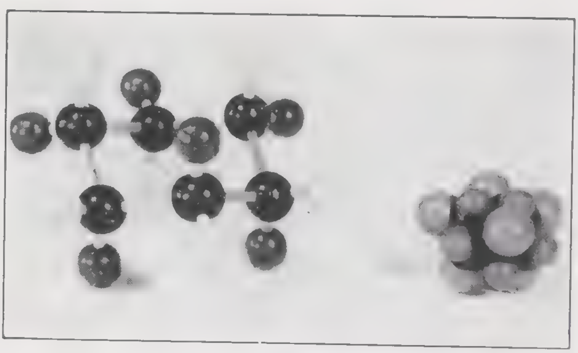
Delta isomer

The beta isomer has been determined by X-ray analysis to be centrosymmetrical, with the six hydrogen atoms pointing alternately upwards and downwards, so that the six chlorine atoms alternating with them all point outwards when arranged on a Fisher or von Bayer centrosymmetrical model. The alpha isomer,

which is considered to be a mixture of two mirror-image molecules, occurs most frequently in preparations of hexachlorocyclohexane. The structure originally postulated for the gamma isomer has one exception to the regular upwards-downwards alternation, so that one hydrogen takes its place, displacing one chlorine atom, in the outer ring[171] (Fig. 8A). More recent determination of crystal structure by X-ray analysis has suggested that the hydrogen atoms on either side of this locus have also been interchanged with chlorine, so that there are now three hydrogen atoms in the outer ring[196] (Fig. 8B). Nevertheless, recent evidence from relative rates of dehydrochlorination indicates the original postulation to be correct. The structure of the delta isomer has also been deduced.[171]



A



B

Fig. 8. Molecular structure of lindane (gamma-hexachlorocyclohexane). *Left:* Chair-type centrosymmetrical model. Carbon atoms black; chlorine, gray; hydrogen, white. *Right:* Fisher centrosymmetrical model. Chlorine atoms large; hydrogen, small. (A. According to Slade; B. according to van Vloten *et al.*)

Of these isomers, gamma-hexachlorocyclohexane, which has been called gammexane and, more correctly, lindane, is by far the most insecticidal. It is 1000 times as toxic as the mixture of isomers (i.e. BHC or benzene hexachloride) to *Sitophilus granarius* by contact, and 10 times as toxic to laboratory rats. The insecticidal activity of benzene hexachloride was found to be attributable purely to its content of the gamma isomer.[112] The median lethal dosage of the gamma isomer to three species of insects was found to lie between 0.4 and 57 mg/kg.[160]

The beta and epsilon isomers are practically non-toxic to insects. The alpha and delta isomers are moderately active, the delta being the more insecticidal for some species but not for others. The delta isomer is more poisonous than the alpha to rats, and is the most toxic of all the isomers to snails. Its insecticidal activity was found to be as follows, in per cent of that of lindane:[96,112,160] *Macrosiphum* 6, *Prodenia* and *Epilachna* 2, *Sitophilus* 1, and *Heliothrips* 0.01.

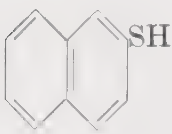
The gamma isomer is readily dehydrochlorinated by alkali to form trichlorobenzenes, while the non-toxic beta isomer is resistant to dehydrochlorination. The trichlorobenzenes themselves are not insecticidal. The heptachloro-, octachloro-, enneachloro-, and hexabromo-cyclohexanes are practically non-toxic.[112]

The molecular configuration of lindane had been postulated to be similar to the analogous hexahydroxycyclohexane, *meso*-inositol, which is a B-complex vitamin. On the analogy that methoxychlor, as well as methyl- and ethyl-DDT, is of the same order of toxicity as DDT itself, the hexamethoxycyclohexane was prepared as the polyether of *meso*-inositol; however, it proved to be much less toxic to flies than lindane. The hexamethyl and hexaethyl cyclohexanes were much less insecticidal than BHC to *Sitophilus*.[103]

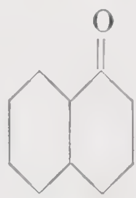
Derivatives of naphthalene

Naphthalene is more toxic than benzene. However, its nitro derivatives are only slightly active, with the exception of α-nitronaphthalene, which is 3 times as toxic as naphthalene.[189] The halogen derivatives are moderately insecticidal, the α-chloro compound being 8 times as toxic as naphthalene, and the β-chloro, bromo, and iodo derivatives being effective against

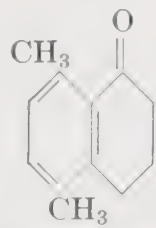
caterpillars.[183] Whereas β-naphthol is practically non-toxic,[40, 109] β-thionaphthol is moderately insecticidal.[22] Although α-naphthylamine is more toxic than aniline,[186] its derivatives are weak as insecticides. The naphthalenesulphonic acids are consistently ineffective. The methylnaphthalenes are quite toxic and are often used as insecticide carriers because of their high solvent power. Naphthoquinone is inactive, but its hydrogenated analogue decalone is effective against *Pediculus*, the alpha-decalone being better than β-decalone or α-decalol. 5,8-Dimethyl-1-tetralone is an excellent lousicide,[40] and α- and β-tetralol are effective insect repellents.[137] Certain alkyl-naphthoquinones, which are effective anti-malarial agents, have shown promise as insecticides and acaricides.



β-Thionaphthol



α-Decalone



5,8-Dimethyl-1-tetralone

The methyl and ethyl ethers of β-naphthol and β-thionaphthol are moderately insecticidal,[180] as also are the α- and β-naphthyl cyanides[15, 189] and α-naphthyl isothiocyanate.[183] None of the many N-naphthyl benzenesulphonamides tested show any toxicity.[167] Of many azo compounds tested, only 1-phenylazo-2-naphthylamine showed a moderate degree of effectiveness.

The naphthalene analogues of DDT, in which the phenyl groups are replaced by naphthyl, are unsuccessful as contact insecticides.[106] Of derivatives of polycyclic hydrocarbons higher than naphthalene, none have been found to show any toxicity except anthraquinone, 9-bromophenanthrene, 9,9-dichlorofluorene, and 9-fluorenone, which were of slight to moderate toxicity only.[183] Like naphthyl-DDT, these molecules are very large.

Derivatives of biphenyl

Biphenyl itself is moderately insecticidal and may be regarded as one of the most toxic of the hydrocarbons. The addition of halogen and amino groups increases its toxicity, whereas nitro

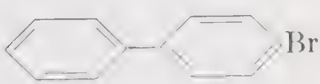
or hydroxy groups decrease it. The data summarized in Table 10 show that substitution in the *para* position yields the most effective derivatives.

TABLE 10. Toxicity of Biphenyl Derivatives

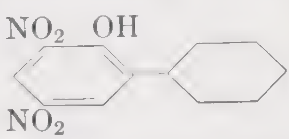
That of biphenyl itself is ++.

Position of Substituent	F	Cl	Br	I	NH_2	NO_2	OH
o		+	+	−	++	+	+
p	++	++	+++	+	+++ to −	+	−
p, p′	+++ to −	+++ to −	−	−	−		

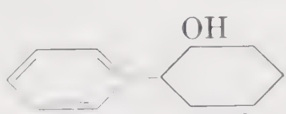
p-Bromobiphenyl proved to be toxic to all the great variety of species on which it was tested. However, both *p,p′*-difluoro- and *p,p′*-dichlorobiphenyl, although effective against leaf-eating insects,[89, 183] were found to be ineffective against *Culex* and *Carpocapsa* larvae.[13, 168] *p*-Aminobiphenyl is poisonous to larvae of *Anopheles*, but not to *Cochliomyia* or *Musca*.[11, 40] The *p*-methoxy and *p*-ethoxy biphenyls are moderately toxic,[15] but the *p*-phenyl-acetophenones and -acetanilides are inactive.



p-Bromobiphenyl



2,4-Dinitro-6-cyclohexylphenol



2-Phenylcyclohexanol

The biphenyl derivative 2,4-dinitro-6-phenylphenol is a good insecticide,[183] and 2,4-dinitro-6-cyclohexylphenol is excellent. This material is known as DNCHP and may be regarded as a derivative of DNOC in which the methyl group is replaced by a cyclohexyl radical. The 4-cyclohexyl- and 2-cyclohexylidene-

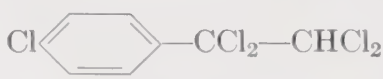
cyclohexanones are quite good lousicides.[40] 2-Phenylcyclohexanol is an acaricide, and along with 2-cyclohexylcyclohexanol is an excellent insect repellent.[137]

Alkyl and acyl benzenes

Toluene shows a certain contact and fumigant toxicity.[186] Chlorination of the methyl group yields benzyl chloride (ϕ-CH_2-Cl), an irritant lachrymator for man, whose vapour has proved to be stimulating to insects such as *Aonidiella*, *Hippodamia*, or *Agriotes*.[138,190] This effect stands in contrast to that of the chlorotoluenes, in which the chlorine is substituted on the benzene ring; their effect on *Aphis* is highly anaesthetic.[189] The benzyl and xylyl bromides are also found to be irritating to *Hippodamia*.[138] However, the actual toxicity of these irritants is erratic if they are employed as fumigants.

Benzyl chloride

p-Nitrobenzyl bromide

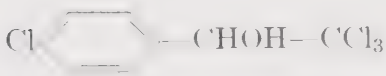


Lucex

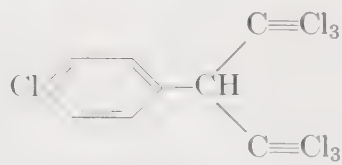
The *o*- and *p*-chlorobenzyl chlorides and benzotrichloride are moderately toxic when added to the insect's food, but none of them are contact poisons.[10,11] Whereas *p*-chlorobenzyl trichloride is inactive, the *m*-chloro isomer shows considerable toxicity to *Anopheles* larvae.[31] As a group, these chlorinated toluenes proved to be ineffective against *Carpocapsa*.[161] The nitrobenzyl chlorides and *p*-nitrobenzyl bromide are toxic to aphids or caterpillars.[183,189]

Whereas ethylbenzene is non-toxic, chlorination of the side-chain of *p*-chloroethylbenzene makes for effective insecticides.[illegible] Of the seven chlorinated derivatives of *p*-chloroethylbenzene or (4-chlorophenyl)-ethane tested on *Sitophilus*, the most effective compound was 1,1,2,2-tetrachloro-2-(4-chlorophenyl)-ethane, which is the active principle in the German insecticide *Lucex*. Relative potency decreases with decreasing content of chlorine in the ethane side-chain, although the completely chlorinated

pentachloro derivative is virtually non-toxic, being also resistant to dehydrochlorination. The corresponding ethylenic compounds were slightly less toxic, and their effectiveness also decreased as the chlorination decreased.[175,203] Similar toxicity results from chlorination or nitration of the unsaturated analogue styrene (ϕ-CH=CH$_2$), whose β-nitro and β-nitroso derivatives, and its α,β-dibromide, are highly insecticidal.[11,183] 1,2-Dibromo-2-nitroethylbenzene is highly insecticidal, and *p*-methoxystyrene is highly toxic to *Pediculus*.[40] Of the many derivatives of β-trichlorophenylethanol tested, the *p*-chloro derivative (known as carbinol-DDT) showed one-fiftieth the residual toxicity of DDT[141] and was not as effective as the *p*-fluoro analogue.[13]



Carbinol-DDT



p-Chlorophenyl-hexachloropropane

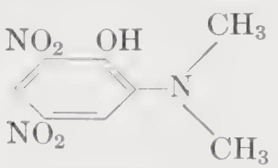
Neither isopropylbenzene (cumene) nor *p*-cymene is insecticidal, but their hydroxy derivatives menthol and thymol have been found to be effective against codling moth and body lice.[40] 2,4-Dinitrothymol has shown high toxicity to *Cochliomyia*[15] and *Bombyx* larvae.[77] The heavily chlorinated *p*-chlorophenyl-hexachloropropane has proved to be a residual poison as toxic as DDT to *Drosophila*;[13] it will be remembered that hexachloropropene and heptachloropropane are highly toxic fumigants.[9]

The derivatives of phenylacetic and cinnamic acids show no toxicity. The phenyl alkyl ketones, however, which contain the C=C—C=O grouping, include several toxic compounds among their derivatives. Of the derivatives of acetophenone (ϕ-CO-CH$_3$), the *p*-methoxy is a good lousicide,[40] and the *p*-amino[181] and 3,4-dichloro[188] derivatives are quite toxic to caterpillars. Chlorination of the ω-carbon of *p*-chloroacetophenone produces compounds of moderate toxicity.[12,141] Moreover, *p*-methoxy- and *p*-ethoxy-propiophenone, *p*-chlorobutyrophenone, and ω-allylacetophenone are good knockdown poisons for *Pediculus*.[40] Anisalacetone is highly toxic to *Cochliomyia* larvae,[15] but not to other species of insects.

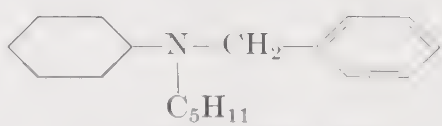
Alkyl anilines

These compounds, which may be regarded as phenyl alkyl imines, are generally of slight toxicity. Whereas the N-alkyl anilines are scarcely more effective than aniline, the N-aryl anilines such as diphenylamine are considerably more insecticidal.

Of the derivates of methylaniline, N-methylanthranilic acid, ϕ-(COOH)—NH—CH_3, is a good lousicide and acaricide. N-methyl- and N-caproylpicramic acid proved to be considerably toxic, and N,N-dimethylpicramic acid highly so, to the caterpillar *Phlyctaenia*.[117] It will be noted that picramic acid bears a structural resemblance to the insecticide DNOC. Both picramic acid and anthranilic acid have a methylamino group in a position *ortho* to the acid radical.



N,N-Dimethylpicramic acid



N,N-Amylbenzyl-cyclohexylamine

N-Nitrosomethylaniline has been found to show considerable toxicity to *Cochliomyia*, *Sitophilus*, and *Pediculus*. Addition of a carboxyl group to the methylamine side-chain produces phenylglycine, whose derivatives are not insecticidal.[183] However, the nitrile of phenylglycine, and several of its derivatives, have given good results against the codling moth.[165] And the somewhat analogous esters, N-methyl- and N-ethyl-N-phenylurethane, are moderately good lousicides.[40]

Hydrogenation of aniline to produce cyclohexylamine results in a sharp increase of contact toxicity. The N-alkyl and acyl derivatives of cyclohexylamine are highly active. Of these, N,N-amylbenzyl-cyclohexylamine is outstanding, being more insecticidal and less phytotoxic than N,N-amylbenzoyl-cyclohexylamine. It is concluded that the acidic groups, benzoyl or acetyl, are mainly responsible for the phytotoxicity of these compounds.[78]

Acyl anilides

All the acyl anilides in the series from formanilide (ϕ-NH-CO-H) to palmitanilide are of negligible toxicity, and the same is true of the analogous N-benzyl amides. Only the 2,6-dimethyl

derivative of formamide is at all insecticidal.[183] None of the many derivatives of acetanilide (ϕ-NH-CO-CH_3) which have been tested are more than slightly toxic. However, the *o*- and *p*- (but not the *m*-) chloro- and bromoacetanilides are of moderate toxicity to caterpillars (Table 11).[180,183] Of the derivatives

TABLE 11. TOXICITY OF HALOGENATED ACETANILIDES

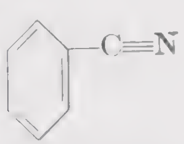
Per cent mortality of Vth-stage *Prodenia eridania* larvae

Position	Fluoro	Chloro	Bromo	Iodo
o	..	90	40	39
m	..	0	0	0
p	63	37	50	0

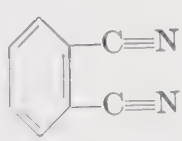
of N-methylacetanilide, the *p*-nitro [15] and *p*-methyl [183] are moderately insecticidal. N-propylacetanilide is toxic to *Cochliomyia*,[15] the N-isopropyl analogue to *Pediculus*,[40] and N-acetyl-N-ethyl-*p*-phenylenediamine and N-caproylpicramic acid are toxic to caterpillars.[117,183]

Aromatic nitriles

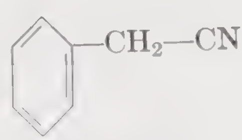
Benzonitrile is a stomach poison but not a contact insecticide.[10,11,189] Of the disubstituted benzenes, *m*-dicyanobenzene is non-toxic;[106] but the *o*-dicyanobenzene, i.e. phthalonitrile, is highly toxic as a stomach poison of caterpillars and dipterous larvae.[110,179]



Benzonitrile



Phthalonitrile



Benzyl cyanide

The toxicity increases in passing up the series from benzonitrile to benzyl cyanide (phenylacetonitrile), decreases again to phenylpropionitrile, but rises with desaturation to styryl cyanide, ϕ-CH=CH—CN (Table 12). Still further up the scale, the unsaturated cyclohexenylallylacetonitrile is a powerful lousicide. Chlorination of benzonitrile or benzyl cyanide in the *para* position also produces good lousicides.[40] The monochloro derivatives of benzyl cyanide represent an increase in toxicity, but the dichloro derivatives are less toxic than the parent compound.

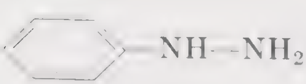
TABLE 12. General and Contact Toxicity of Aromatic Nitriles[10,11]

	General Toxicity, m.l.c. in ppm		Contact Toxicity, m.l.d. in $\mu g/cm^2$		Order of Toxicity to 6 spp.
	Musca	*Sitophilus*	*Blattella*	*Oncopeltus*	
Benzonitrile	400	1700	Neg.	Neg.	6
Benzyl cyanide	310	660	35	Neg.	4
o-Chlorobenzyl cyanide	270	580	55	Neg.	2
p-Chlorobenzyl cyanide	640	200	80	320	1
2,4-Dichlorobenzyl cyanide	550	110	430	Neg.	3
3,4-Dichlorobenzyl cyanide	750	590	100	Neg.	7
β-Phenylpropionitrile	780	940	105	Neg.	8
Styryl cyanide	1300	107	120	Neg.	5

Nitration of benzyl cyanide to *p*-nitrophenylacetonitrile increases the toxicity to *Sitophilus* adults but decreases it to *Musca* larvae; it was observed that the former were more susceptible to compounds containing nitro groups, and the latter to nitriles.[10,11]

Phenyl-substituted nitrogenous compounds

Phenylurea and phenylthiourea, along with their derivatives that have been tested, have proved to be of slight toxicity to insects.[15,72] Phenylhydrazine was found to be highly poisonous to *Cochliomyia* larvae and to *Sitophilus* adults. Of its derivatives by substitution of the benzene ring, only the 2,4-dinitro was as good as phenylhydrazine itself,[15] although it was ineffective against *Carpocapsa*.[168] However, many phenylhydrazides were found to be distinctly toxic, notably those of isobutyric, isocapric, valeric and isovaleric, benzoic and benzenesulphonic acids.[7,51]



Phenylhydrazine

1-Phenyl semicarbazide

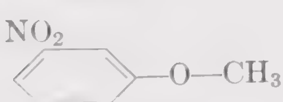
The semicarbazones of cyclohexanone and 2-methylcyclohexanone are moderately insecticidal, and the 4-methylcyclo-

hexanone semicarbazone shows contact toxicity to caterpillars.[180,182] Phenyl semicarbazide and thiosemicarbazide are moderately poisonous to lepidopterous larvae. The semicarbazones of benzaldehyde and acetophenone derivatives show no toxicity, with the exception of *p*-chloroacetophenone semicarbazone, which is effective against codling moth and other caterpillars.[166,180] The oxime of acetophenone, ϕ-C(CH_3)=NOH, is toxic to caterpillars, and its *p*-methyl and *p*-methoxy derivatives are good ovicides for *Pediculus*.

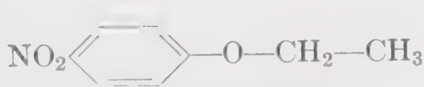
Phenyl alkyl ethers

Anisole, or methyl phenyl ether, is only slightly insecticidal, and its halogen and hydroxy derivatives are no better.[15] However, the nitro derivatives, and particularly *m*-nitroanisole, show high toxicity to *Cochliomyia* larvae, although not to all insects. The best of the amino derivatives, *p*-anisidine (NH_2-ϕ-OCH_3), is moderately insecticidal.[183] Anisonitrile is a fair lousicide.[40] *p*-Anisaldehyde shows considerable toxicity to maggots and lice, and so does its oxime to caterpillars.[183] The carboxyl derivatives of anisole, the phenoxyacetic acids, are not insecticidal; but 2,4-dichlorophenoxyacetic acid (the weedicide 2,4-D) shows slight contact acidity to *Blattella*. Of the cyclohexoxyacetic acids, N,N-diethyl-α-cyclohexoxyacetamide has proved one of the most powerful synergists for DDT-pyrethrum mixtures.[94]

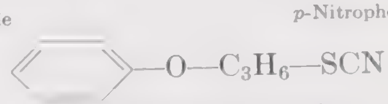
Phenetole, or ethyl phenyl ether, is slightly insecticidal; its halogenated derivatives, of which the best is the *p*-iodo, are a little more active. *p*-Nitrophenetole is very toxic to *Cochliomyia* larvae and has proved to be an excellent protector of wounds against myiasis.[133] The amino derivatives (phenetidines), including their N-acetyl derivatives, are ineffective. Combination of a toxic aldehyde group with the liposoluble ethoxy group produces quite good lousicides in the form of *o*- and *p*-ethoxybenzaldehyde.[40]



m-Nitroanisole



p-Nitrophenetole



γ-Thiocyanopropylphenyl ether

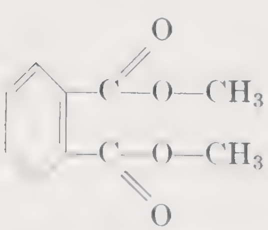
Many of the higher alkyl phenyl ethers have shown effectiveness as lousicides; these include derivatives (generally *p*-substituted) of the phenyl ethers of isopropyl, propyl, propylene oxide, allyl, isobutyl, butyl, and amyl groups.[40] Isobutenyl phenyl ether also shows high insecticidal activity.[89] Of the alkyl ethers of pentachlorophenol, toxicity was found to rise in the series to reach a peak at amyl pentachlorophenyl ether, which however, was scarcely more toxic to *Musca* or *Attagenus* than pentachlorophenol itself.[199] The phenyl ethers of thiocyanoethyl and thiocyanopropyl radicals are very toxic to *Aphis rumicis*.[67]

A number of benzyl ethers of methyl, ethyl, and allyl alcohols are toxic to *Pediculus*. The best is 2-amino-1-phenylethyl ethyl ether, ϕ-$CH(OC_2H_5)$-CH_2-NH, an excellent lousicide. The ethoxy-*p*-chlorophenyl analogue of DDT has shown moderate residual toxicity.[12]

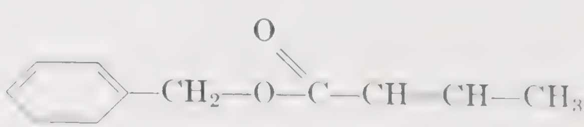
Aromatic esters

Aromatic acid with aliphatic alcohol. Benzoic acid, phenylacetic acid, and their higher homologues, and the cyclohexyl fatty acids, are not insecticidal. The only esters of benzoic acid derivatives to show toxicity are: the salicylates (OH-ϕ-COOO-), moderately toxic to *Pediculus* and *Carpocapsa*,[109] the anthranilates (NH_2-ϕ-COO-), the methyl and *sec*- and *tert*-butyl esters being most toxic; and the anisates (CH_3O-ϕ-COO-), whose methyl ester is toxic to *Pediculus*.[40]

The esters of the dibasic phthalic acid, dimethyl phthalate (DMP) and dibutyl phthalate (DBP) are excellent acaricides and mosquito repellents, and DBP exerts synergistic action with pyrethrins.



Dimethyl phthalate

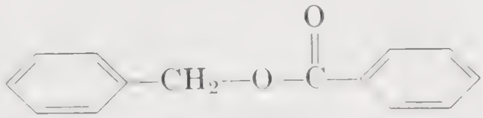


Benzyl crotonate

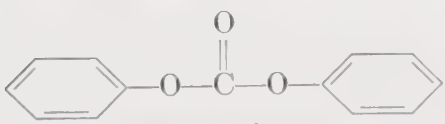
Aromatic alcohol with aliphatic acid. The benzyl and phenylethyl esters of acetic and other fatty acids are of negli-

gible toxicity.[93] However, benzyl crotonate and phenylethyl butyrate are good lousicides,[40] and the propionates of DNP and DNOC are toxic to lice and caterpillars.[182] Dinitrocapryl phenyl crotonate is an effective ovicide and miticide that has been commercially marketed as *Arathane*.

Aromatic acid with aromatic alcohol. Phenyl benzoate, benzyl benzoate, and the cresyl benzoates are excellent acaricides, highly toxic to trombiculid mites (chiggers) but not to the plant-feeding tetranychid mites or to insects.[15,183] However, *p*-chlorobenzyl *p*-chlorobenzoate is quite poisonous to *Paratetranychus*.[113]



Benzyl benzoate

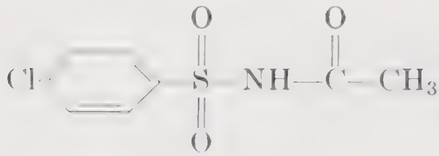


Diphenyl carbonate

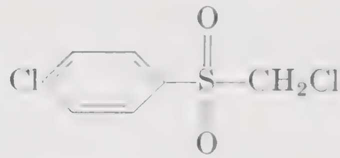
Carbonates and oxalates. Certain of the aryl alkyl carbonates are of considerable toxicity to insects. The ethyl *p*-chlorophenyl, *p*-tolyl, and benzyl carbonates are good lousicides,[40] and the ethyl 4-methyl-2-chlorophenyl and 2-methyl-1,4-dichlorophenyl carbonates are good mosquito larvivides. Although diphenyl carbonate is slightly insecticidal (and highly acaricidal), its derivates are ineffective. The oxalates, with the exception of *p*-dimethylaminophenyl oxalate, are of negligible toxicity to insects.

Aromatic compounds of sulphur

Benzenesulphonamides. Like benzenesulphonic acid, benzenesulphonamide (ϕ-SO_2-NH_2) and most of its derivatives are of negligible toxicity. However, the *p*-chloro- and *p*-bromobenzenesulphonamides are moderately toxic.[183] The N-alkyl benzenesulphonamides also are ineffective, with the exception of the N-ethyl and N-propyl derivatives of *p*-bromobenzenesulphonamide.[162,182] The N-acetyl derivative of *p*-chlorobenzenesulphonamide is effective against the clothes moth.[59]



N-Acetyl-*p*-chloro-benzenesulphonamide



p-Chlorophenyl chloromethyl sulphone

p-Chlorobenzyl thiocyanate

Sulphones. Phenyl chloromethyl sulphone is a promising insecticide for screwworm larvae and is a persistent poison for lice and their eggs. The *p*-chloro derivative is also a good lousicide, having seen general use in Germany under the name *Lauseto-Neu;* however, it shows only one-quarter the toxicity of DDT.[21] It is of slight value against other insects, with the exception of bedbugs. The *p*-methoxy derivative is toxic to *Cochliomyia*, and 3,4-dichlorophenyl hydroxymethyl sulphone is highly toxic to *Cimex*.

Sulphides. Other phenyl sulphur compounds, including phenyl alkyl sulphides, phenyl sulphuramines (ϕ-S-NH_2), benzenesulphonates, and derivatives of thiophenylacetic acid, are of negligible toxicity.

Thiocyanates. Although phenyl thiocyanate is only slightly insecticidal, its *p*-amino derivative is an effective contact poison.[67] The *p*-chloro and *p*-bromo derivatives also are highly toxic, slightly surpassing *p*-iodophenyl thiocyanate.[183] Benzyl thiocyanate has shown high contact toxicity to *Aphis, Blattella*, and *Sitophilus*.[10, 67]

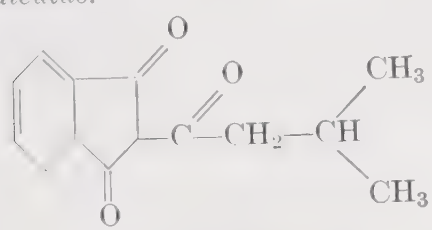
TABLE 13. General and Contact Toxicity of Benzyl Thiocyanate and Chlorinated Derivatives[10,11]

	General Toxicity m.l.c. in ppm		Contact Toxicity, m.l.d. in $\mu g/cm^2$	
	Musca	*Sitophilus*	*Blattella*	*Oncopeltus*
Benzyl thiocyanate	230	68	35	80
o-Chlorobenzyl thiocyanate	410	60	45	55
p-Chlorobenzyl thiocyanate	700	94	30	33
2,4-Dichlorobenzyl thiocyanate	1600	640	380	50
3,4-Dichlorobenzyl thiocyanate	Neg.	Neg.	Neg.	70

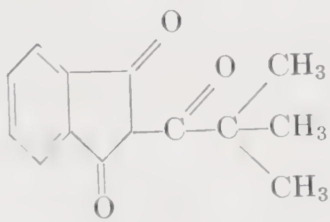
Monosubstitution with chlorine increases the contact effectiveness but disubstitution decreases it (see Table 13). *p*-Chlorobenzyl thiocyanate, the most toxic of the derivatives, is more insecticidal than DDT to *Blattella* by direct contact.

Cyclopropane and cyclopentane derivatives

Cyclopropane, which contains three carbon atoms linked in a ring, is a powerful narcotic. It is a component of the molecules of pyrethrins and cinerins. When it was used to replace the trichlorethane nucleus of DDT, a contact insecticide of outstanding effectiveness was obtained. The alkyl ethers of cyclopropane showed moderate fumigant toxicity to *Tribolium*.[149] Two esters with cyclopropane in the molecule were toxic to *Pediculus*.[40]



Valone



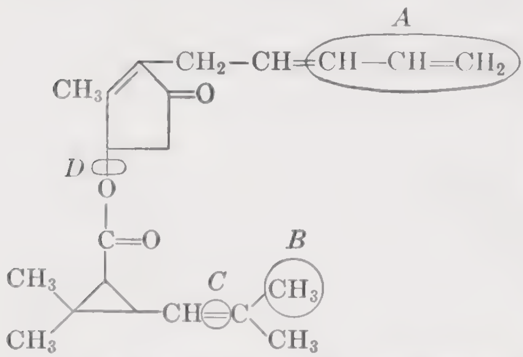
2-Pivalyl-1,3-indandione

Cyclopentane, a naphthene with a five-membered ring, is virtually non-toxic to insects. Cyclopentanone also is ineffective, but its semicarbazone was found to be moderately insecticidal.[180] Aromatic derivatives of cyclopentanone showed no activity,[183] with the exception of 2-(1-cyclopentenyl)-cyclopentanone, which was markedly toxic to *Pediculus*. Several derivatives of indandione, or benz-cyclopentanone, were also good lousicides. The most outstanding were 2-isovaleryl- and 2-pivalyl-1,3-indandione, known, respectively, as the insecticides valone and *tert*-butyl valone.

Pyrethrins

The highly insecticidal pyrethrins are esters of an acid containing a cyclopropane ring with an alcohol containing a cyclopentane ring. After the discovery that pyrethrum extracts consisted not only of pyrethrins I and II, but also cinerins I and II, there being two ketonic alcohols as well as two chrysanthemum acids, steps were taken to synthesize each of the four com-

pounds, and to prepare derivatives hydrogenated at the two, or three, double bonds.[86] Tests of the contact toxicity of these compounds to *Musca* adults have revealed that none of the analogues are as powerfully insecticidal as pyrethrin I.[50] Hydrogenation or substitution at any one point results in a decrease in toxicity which is similar whatever the analogues concerned. The results may be considered in terms of change of the pyrethrin I molecule, whose graphic formula is given below with the esterified hydroxyl group of pyrethrolone placed in the 4 position in the light of recent work.[88]



pyrethrin I, ester of {pyrethrolone and chrysanthemum monocarboxylic acid}

1. Replacement of CH—CH$_2$ at point *A* by CH$_3$ yields cinerin I, which is two-thirds as toxic as pyrethrin I. With a similar replacement, cinerin II is two-thirds as toxic as pyrethrin II.

2. Replacement of CH$_3$ at point *B* by COOCH$_3$ yields pyrethrin II, which has one-quarter the toxicity of pyrethrin I. With a similar replacement, cinerin II shows one-quarter the toxicity of cinerin I.

3. Saturation of the double bond at point *C* yields isodihydro-pyrethrin I, one-half as toxic as pyrethrin I. Similarly hydrogenated, isodihydro-cinerin I is one-half as toxic as cinerin I.

4. Saturation of the double bond at point *C* in either pyrethrin II or cinerin II yields isodihydro derivatives of negligible toxicity.

5. Saturation of the two double bonds of the side-chain results in a 94% loss of toxicity.

6. With cinerin I, removal of the point of esterification (*D*) to the 5 position on the cyclopentene nucleus, or of the butenyl side-chain to the 3 position on that nucleus, results

in compounds of one-eighth the toxicity of cinerin I, where esterification is at the 4 position and the butenyl side-chain is in the 2 position.[87]

7. Hydrolysis of the ester linkage at point *D* liberates the component alcohols (pyrethrolone and cinerolone) and acids (chrysanthemum monocarboxylic acid and dicarboxylic acid, methyl ester), which are not toxic. It has been shown that restoration of the ester linkage by esterification of chrysanthemum monocarboxylic acid with lauryl, myristyl, or cetyl alcohol, or with diethanolamine, produces compounds which show 90% of the insecticidal activity of the intact pyrethrins, but fail to produce the characteristic symptoms of pyrethrum poisoning.[68]

Previous work has shown that pyrethrin I (including cinerin I) is more toxic than pyrethrin II (with cinerin II) to *Aphis*[191] and *Blattella* as well as to *Musca*.[55,56] However, pyrethrin II is far superior to pyrethrin I in its knockdown power for adult houseflies.[177]

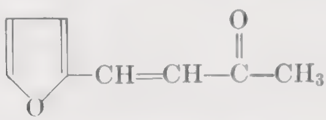
Esterification of chrysanthemum monocarboxylic acid with a *p*-chlorophenyl group, in an attempt to get a pyrethrum-DDT "hybrid" compound, resulted in a moderately toxic compound. Substitution of the *p*-chlorophenyl group on a pyrethrolone derivative did not induce any significant toxicity.[66]

Recently the substitution of allyl ($—CH_2—CH{=}CH_2$) and isobutenyl ($—CH_2—(CH_3)C{=}CH_2$) groups in the side-chain of cinerolone and its esterification with chrysanthemum monocarboxylic acids have yielded synthetic pyrethrin analogues (e.g. allethrin) which are more toxic to houseflies than mixed pyrethrins of natural origin.[154]

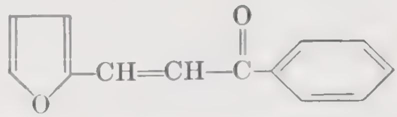
Heterocyclic compounds with O in the ring

Furan and other five-membered rings. Out of a large number of derivatives of furan that have been tested, including many with aromatic substituents, very few have shown insecticidal activity. These few are furfurylideneacetone, allylfurfurylidene acetate, furylacrylamide[180] and ethyl furfurylacetoacetate,[89] all of which contain an $O—C—C{=}C—C{=}O$ configuration. It was thus surprising to find that the furalacetophenones, where this grouping is attached to a benzene ring, were not toxic. How-

ever, N-(2-furfurylidene)-*o*-toluidine, with an O—C—C=N grouping, was active against *Pediculus*.[40]



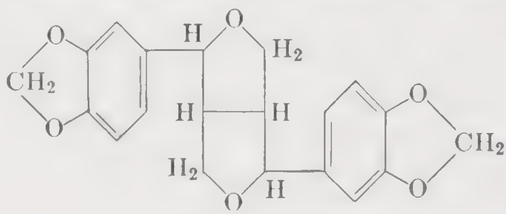
Furfurylideneacetone
(*Toxic*)



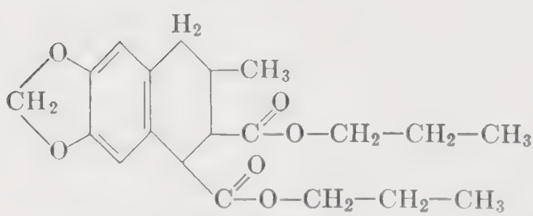
Furalacetophenone
(*Non-toxic*)

Benzofuran and phthalic anhydride are compounds containing both furan and benzene rings. Benzofuran was virtually ineffective against insects;[126] and while phthalic anhydride was slightly toxic, its derivatives were not insecticidal.

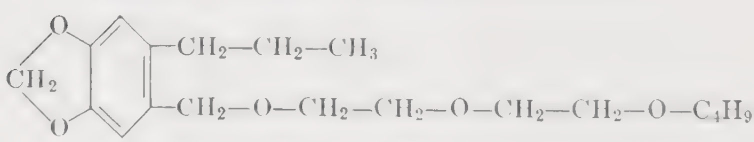
Methylenedioxyphenyl compounds. The methylenedioxyphenyl group, consisting of a five-membered ring with two oxy-



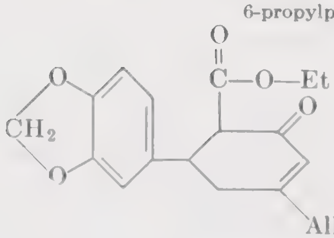
Sesamin

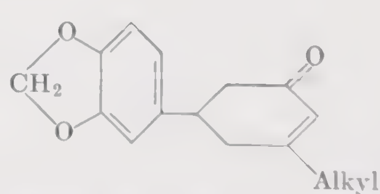


n-Propyl isome
(*Condensation product of propyl maleate with isosafrole*)



"Piperonyl butoxide" or
6-propylpiperonyl-butylcarbityl ether





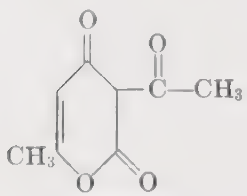
"Piperonyl-cyclohexenone" or "piperonyl-cyclonene"

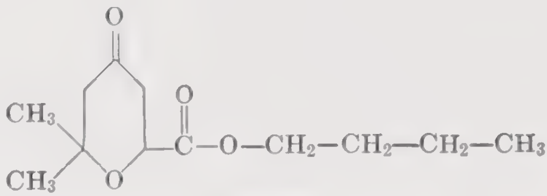
gen atoms, attached to a benzene ring, is found in a number of compounds of high biological activity. Although piperonal is biologically inactive, derivatives with an α,β-unsaturated side-chain, such as fagaramide and piperine, are highly insecticidal. Piperine, the piperidide of piperic acid, has proved to be more toxic than pyrethrins to houseflies.[69] The amides and esters of piperic acid also show exceptional toxicity. The N-substituted amides and other derivatives of the related methylenedioxyphenyl-acrylic acid are contact poisons for houseflies.[184] Piperonylacetonitrile is a good lousicide, and is also ovicidal.[10] The thioethers, sulphoxides, and sulphones of safrole (1-allyl-3,4-methylenedioxybenzene) are very active.[185]

These piperonal derivatives with their methylenedioxyphenyl groups are most effectively employed as synergists for pyrethrum. The first to be discovered was sesamin, which has two such groups; pinoresinol, a compound lacking these groups but otherwise similar, has no synergistic effect.[60] Further work established that other methylenedioxyphenyl compounds, such as piperine, fagaramide, methylenedioxyphenol-cinnamamides, N-substituted piperonylamides, and *n*-propyl isome, were effective synergists for pyrethrum.[184] It was later found that excellent synergists could be found in the mixture of compounds formed by condensation of alkyl-3,4-methylenedioxystyryl ketones with ethyl acetoacetate. This material consisted to the extent of 80% of the two compounds shown above, and has been termed "piperonyl-cyclohexenone" or "piperonyl-cyclonene." A compound with even better synergistic and solubility properties was found in the diethylene glycol ether of butyl alcohol and 3,4-methylenedioxy-6-propylbenzyl alcohol, which was termed "piperonyl butoxide."[197] Of a total of 3800 compounds tested, 1-(3,4-dioxymethylenephenyl)-2-methyl-1,3-propanediol methylene ether was one of the five compounds that showed outstanding synergistic properties with pyrethrum against *Musca* and *Anopheles*.[94]

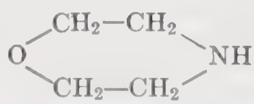
Pyran and other six-membered rings. This group contains dehydroacetic acid, an excellent poison for clothes moths and for leaf-eating caterpillars.[59,180] Other pyrandione and pyranone derivatives were found to be non-toxic. Another derivative is the mosquito repellent indalone, which exhibits the C=C—C=O

grouping, is toxic to houseflies and mosquitoes, and is a bactericide and fungicide.[48]


Dehydroacetic acid


Indalone

The toxicity of the benzpyranone derivatives, coumarin and benzotetronic acid, has been discussed elsewhere. Coumarin is moderately toxic when mixed with the insect's food medium but has no contact efficacy.[10,11] Substitution of S in the carbonyl groups produces 2-thiocoumarin, which shows considerable toxicity to caterpillars and is one of the best deterrents for *Carpocapsa*.[168] The 3-ethyl- and 3-acetylcoumarins are moderately good insecticides, while the 3-acetyl and 3-carbethoxy derivatives of benzotetronic acid are very good.[89]

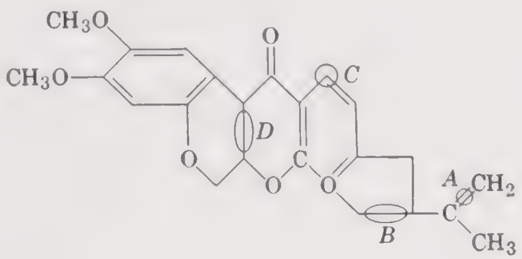

Morpholine

Morpholine, consisting of a 6-membered ring which contains an amino group and an ether linkage, is an insect fumigant of quite high toxicity.[9] It is remarkable that the derivatives of morpholine are ineffective against most insects; none showed contact toxicity and only two showed any kind of insecticidal activity.[10,11] However, dodecylmorpholine and N-benzylmorpholine have been found to be lousicidal.[40]

Derivatives of rotenone and deguelin

Rotenone. The molecule of rotenone may be regarded as a combination of a centrally placed γ-pyrone ring flanked on either side by a benzopyran and a benzofuran configuration. Each ring has lost one double bond, and the benzopyran bears two methoxy groups and the benzofuran a 2-propenyl group. Although rotenone contains three asymmetric carbons and could

exhibit *cis-trans* isomerisms at point *C*, only the laevo isomer is known. Research has elucidated the effects upon toxicity of modification of this molecule.



1. Saturation of the double bond at point *A* yields dihydrorotenone. This is slightly more toxic than rotenone to *Culex* larvae,[76] and one-third as toxic to *Bombyx* larvae.[158] It is 1.5 times as toxic to goldfish as rotenone.[49]

2. Transference of the double bond at point *A* to a point inside the furan ring at point *B* yields isorotenone. This compound is one-third as toxic to *Culex* larvae as rotenone, and when in racemic mixture its toxicity is reduced to one-fifth.[12] It is 0.25 times as toxic as rotenone to goldfish.

3. Substitution of a hydroxy group at point *C* yields sumatrol, a constituent of derris extract. Its toxicity to insects has not yet been tested, but it is considered to be probably less than that of rotenone.

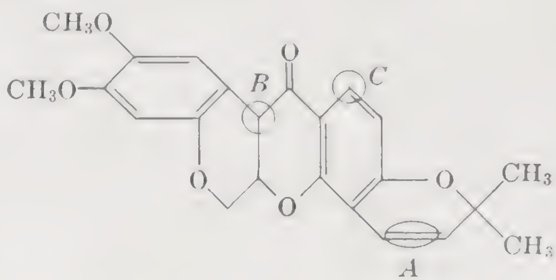
4. Introduction of a double bond at point *D* by mild oxidation yields dehydrorotenone. This is slightly toxic to insects, as judged by its effect on *Bombyx* larvae.

5. Further oxidation produces rotenonone and derric acid.[45] Alkaline degradation produces the cleavage products, rotenol, derritol, and tubaic acid.[157] These compounds are scarcely toxic to insects.[158]

TABLE 14. Toxicity of Rotenone and Deguelin Derivatives to Animals

	Aphis [33]	*Bombyx* [158]	Goldfish [49]	Guinea Pig [2]
Rotenone	100	100	100	100
Deguelin	10	28	39	1
Tephrosin	2.5	6.6	15	Untested
Toxicarol	0.25	0.2	55	12

Deguelin. This compound differs from rotenone in possessing a second benzopyran ring instead of the benzofuran ring. Its stomach toxicity is one-quarter that of rotenone to *Bombyx* larvae,[158] and its contact toxicity one-tenth that of rotenone to *Aphis rumicis*.[33] So far as vertebrates are concerned, deguelin shows 40% of the toxicity of rotenone to goldfish,[49] and only 1% to guinea pigs when orally administered (see Table 14).[2] Accompanying rotenone and deguelin in derris and cube roots are two hydroxy derivatives, tephrosin and toxicarol, tephrosin being considered an oxidative product formed during storage. The effect of molecular changes upon toxicity in the deguelin molecule may be summarized as follows:



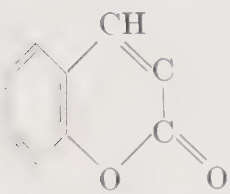
1. Saturation of the double bond at point *A* yields dihydrodeguelin, which is more toxic than deguelin. The optically active isomer of this compound is 5 times as larvicidal to *Culex* as the racemic mixture.[42]
2. Mild oxidation resulting in the substitution of a hydroxy group at point *B* yields tephrosin. This derivative shows one-quarter the toxicity of deguelin both to *Bombyx* larvae *per os* and to *Aphis* by contact. It is 40% less toxic than deguelin to goldfish.
3. Substitution of a hydroxy group at point *C* yields toxicarol, which shows one-fortieth the toxicity of deguelin to *Bombyx* larvae and to *Aphis rumicis*. However, it is 60% more toxic than deguelin to goldfish, and it is 12 times as toxic as deguelin to guinea pigs.[2]

Relation of carbonyl, lactone, and ether groups to toxicity

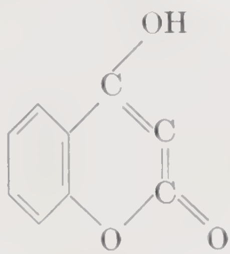
A great number of insecticides are characterized by the possession of carbonyl (C=O) groups, often adjacent to an ether linkage (—O—) or lactone ring. This has prompted a body of speculative ideas on the relation of structure to toxicity that

demands mention if only for the importance of the insecticides involved.

It was noted that coumarin and benzotetronic acid, which contain a carbonyl group attached to a lactone oxygen and adjacent to an ethylenic linkage, were potent mammalian and fish poisons.[39] They could be made insecticidal by the substitution of an acetyl group on the ethylenic bond:

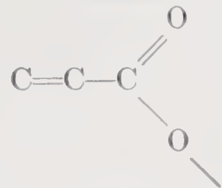


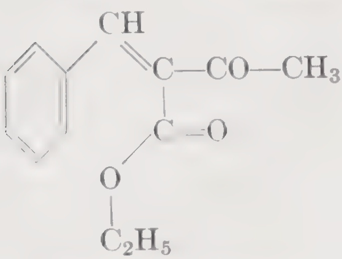
Coumarin



Benzotetronic acid

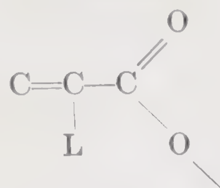
Not insecticidal



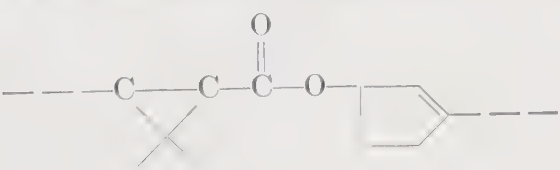


Ethyl benzalacetoacetate

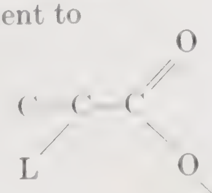
Insecticidal



It was concluded that the substitution of the acetyl group (L) had conferred liposolubility on the molecule and thus allowed it to penetrate the cuticle and act as a contact insecticide. It was further suggested, on highly speculative grounds, that the toxic grouping was present in the pyrethrins at the point where the ester linkage was adjacent to the cyclopropane ring, i.e.

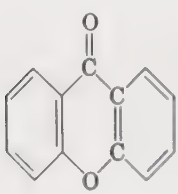


is taken as equivalent to

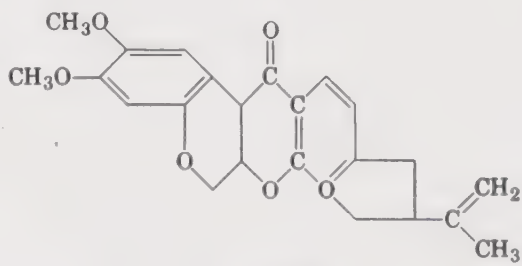


on the grounds that the cyclopropane ring acted as a strongly unsaturated group and at the same time conferred excellent lipoid solubility.[89]

Similar groupings may be discerned in rotenone and xanthone. They merit attention, but the reader must regard any suggestion with a critical eye. In the insecticide xanthone the cyclic oxygen —O— occurs as an ether linkage, not as a lactone. Instead of being attached directly to the carbonyl group it is separated from it by two carbon atoms, i.e. at the opposite end of the C═C—C═O configuration. Nevertheless it would appear that the benzene rings serve as liposoluble groups. A similar configuration is found in rotenone, where the benzofuran and benzopyran rings, with their isopropenyl and methoxy substituents, act as effective lipoid solubilizers.



Xanthone



Rotenone

Therefore for xanthone and rotenone the relation of toxic grouping to lipoid substituents may be represented thus:

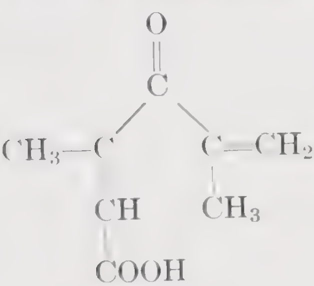
$$\begin{array}{l} L—O—\underset{}{C}—\underset{\substack{|\\ L}}{C}=\underset{\substack{|\\ L}}{C}—C=O \end{array}$$

It is considered that the hydrogen atoms on the carbons of the central ring are also important, since their removal to form dehydrorotenone abolishes the toxicity, and enolization with the keto group greatly decreases it.[102] The toxic O—C—C═C—C═O grouping, with the carbonyl and ether groups separated by three carbon atoms, is shown by the insecticidal compound furfurylideneacetone and its derivatives.

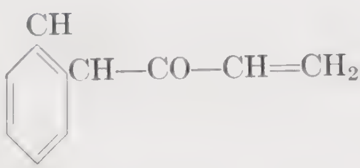
It is of interest that the derivative of benzotetronic acid known as 4-hydroxycoumarin carboxylic acid-3 is not only an excellent insecticide but also one of the most promising fungicides. An

explanation of the relation of toxicity to the structure of this molecule that has been advanced by plant pathologists is that the $\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\!-\!\mathrm{O}\!-\!\mathrm{R}$ substituent, as also the $\overset{\mathrm{O}}{\overset{/\!/}{\mathrm{C}}}\!-\!\mathrm{R}$, has the capacity to withdraw electrons from the ethylenic double bond; and that the more acidic the substituent, the greater its capacity to do so.[111] Thus the toxicity of the C=C—C=O linkage is assignable to the activating power of the C=O group on the adjacent C=C double bond. In the case of 4-hydroxycoumarin carboxylic acid-3, it must be remembered that a second $\mathrm{C}\langle^{\mathrm{O}}_{\mathrm{O}}$ group lies adjacent to the C=C ethylenic linkage in the coumarin ring itself.

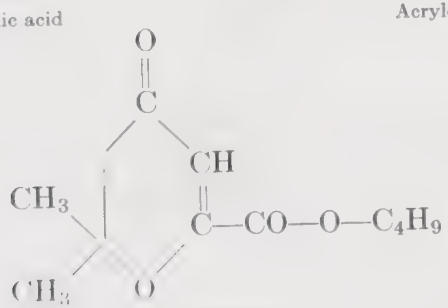
A similar conclusion was reached in the study of analogues of penicillin. Certain synthetic α,β-unsaturated ketones, especially acrylophenone and indalone (a repellent), were found to resemble penicillic acid in being potent poisons for bacteria and fungi. Since their toxic action could be inhibited by protective doses of cysteine or thioglycolic acid, and since they reacted *in vitro* with SH compounds, it was concluded that the toxicity of



Penicillic acid



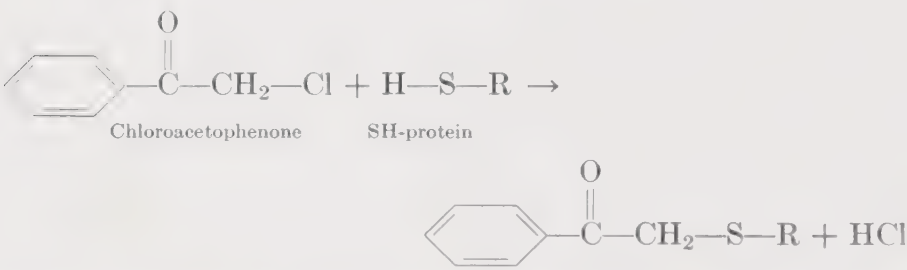
Acrylophenone



Indalone

compounds possessing a C=C—C=O group is correlated with their ability to combine with SH groups.[18] This C=C—C=O grouping is also shown by the highly insecticidal compound piperine; by anisalacetone, which is highly toxic to maggots; by the fumigants acrolein, crotonaldehyde, mesityl oxide, allyl formate, and ethyl acrylate; and by the louse ovicides diallyl succinate and diallyl fumarate.

Strongest evidence of the ability of the carbonyl group in ketones, aldehydes, and esters to activate an adjacent ethylene linkage is offered by the lachrymators used in chemical warfare.[37] Here, just as the carbonyl group activates the adjacent halogenated carbon atom (as in chloroacetone, bromoacetone, bromomethylethyl ketone, and chloroacetophenone) to react with SH groups:



Chloroacetophenone SH-protein

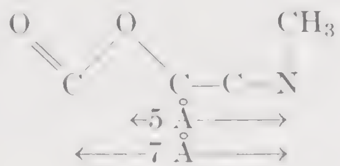
so it activates an adjacent ethylenic group (as in acrolein and acrylate and iodacetate esters) to react with SH groups without the facilitation of a "positive halogen," since the =CH$_2$ becomes positive enough, by withdrawal of electrons, to react with the electronegative S atom.

$$\underset{\text{Acrolein}}{H{-}\overset{\overset{O}{\|}}{C}{-}\overset{\overset{CH_2^{+}}{\|}}{CH}} + \underset{\text{SH-protein}}{\overset{^{-}S{-}R}{\overset{|}{H}}} \rightarrow H{-}\overset{\overset{O}{\|}}{C}{-}CH_2{-}CH_2{-}R$$

The ability of these lachrymators to combine with SH groups in proteins makes them potent inhibitors of such enzymes as succinic and triosephosphate dehydrogenases, hexokinase, xanthine oxidase, and urease, whose activity depends on their SH groups. In mammals these lachrymators show their most pronounced effect on the corneal nerve endings of the eye. The concentration required for nervous stimulation has been found to be of

the same order as that required to poison the enzymes mentioned, an observation that may indicate a connection between the pathology of nerve impulses and the inhibition of specific enzymes.

The importance of the carbonyl group in determining pharmacological action has also been deduced in a study of the spatial configuration of stimulants and depressants of the parasympathetic system of mammals.[135] In acetylcholine the following configuration is present:



where the distance from the carbonyl group to the CH_3 group attached to nitrogen, measured on Hirschfelder atomic models, is approximately 7 Å, and from the oxygen to the N-methyl group is 5 Å. The same distances between carbonyl, oxygen, and methyl groups may be detected in the other stimulants pilocarpine, muscarine, and eserine (Fig. 9). In addition, this spatial configuration may be found in the depressant atropine, where it is placed at the centre of an umbrella-shaped molecule. It has been suggested that atropine exerts its depressant effect by blocking the appropriate receptors from contact with the normal stimulant acetylcholine, which has a smaller molecule. All these parasympathetic stimulants and depressants have an effect on the insect's central nervous system.

Carbonyl (C=O) groups are present also in the insecticide valone (2-isovaleryl-1,3-indandione), which contains three of them.[80] Ether linkages are present in *Lethane 384* (butoxythiocyanodiethyl ether), where there are two in a similar long chain, and in dichloroethyl ether, where the ether linkage occupies a central position.

The radicals C=O, —O—, or C—O are also present, in a central position between two benzene rings, in a number of the most effective acaricides, such as benzyl benzoate, benzil, DCPM, and *p,p′*-dichlorodiphenyl ether. The carbonyl group of unsaturated

aldehydes such as citronellal, and the C=O present in the carboxyl group of esters of phthalic, adipic, and citric acids, are characteristic of compounds repellent to adult mosquitoes. Unsaturated alcohols and saturated diols are also effective repellents.[14, 24]

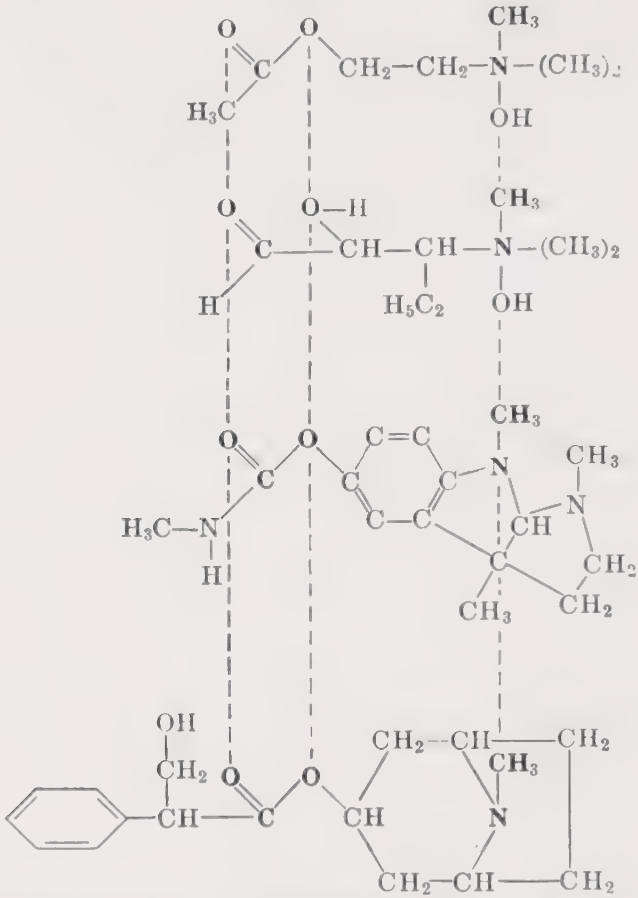
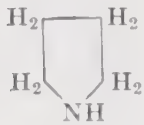


FIG. 9. Structural formula of acetylcholine, muscarine, eserine, and atropine. Markers show carbonyl, oxygen, and N-methyl groups and the distances between them. (From Pfeiffer)

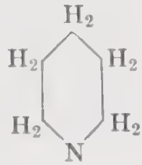
Heterocyclic compounds with N in the ring

Five-membered ring. Pyrrole itself is scarcely insecticidal, but its hydrogenated derivatives pyrroline and pyrrolidine show contact toxicity. Of the derivatives of succinimide, the N-amyl is toxic to *Pediculus*. The addition of alkyl groups to pyrrolidine results in an increasing activity in the order methyl < ethyl <

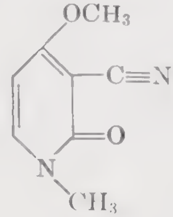
amyl < benzyl. It has been noted that the increase in contact toxicity is paralleled by an increase in the dissociation constant



Pyrrolidine



Piperidine



Ricinine

of these basic compounds[27] (Table 15). A similar relationship has also been observed in testing the analogous N-methyl-acridines as bactericides, where the derivatives with a high dissociation constant ($pK > 7.6$) were found to be at least 3 times as toxic as those with a low alkaline dissociation.[153]

TABLE 15. Toxicity and Dissociation Constant of Substituted Pyrrolidines

Compound	Fumigant on *Tribolium:*[27] LC_{50}, mg/litre	Contact on *Aphis:*[145] LC_{95}, % spray	Dissociation Constant, pK
Pyrrolidine	1.1	1.0	2.89 *
N-Methylpyrrolidine	9.5	1.0	3.82
N-Butylpyrrolidine	1.7	0.5	3.64
α-Phenylpyrrolidine	0.24	0.5	4.40
β-Pyridyl-methyl-pyrrolidine †	0.03	0.01	6.95

* pK 2.89 or dissociation constant 1.3×10^3.

† I.e. nicotine.

Six-membered ring. Pyridine, although acaricidal to some mites[186] and a good fumigant by virtue of its basicity,[82] is not a contact insecticide. Hydrogenation of pyridine yields piperidine, a compound with appreciable contact toxicity to insects,[157] and high toxicity to their eggs.[172] The alkaloid coniine or 2-propylpiperidine, a powerful mammalian poison, was not found to be a contact insecticide.[186] Four piperidine derivatives, including the N-dodecyl, are highly effective lousicides.[10] The aminopyridines show moderate toxicity. Higher insecticidal action is shown by β-cyanopyridine, whose derivatives are

mediocre with the exception of ricinine, which is an outstanding poison for the codling moth.[170]

TABLE 16. Toxicity of Alkyl Derivatives of Pyridine

Alkyl Substituent	Fumigant on *Tribolium*,[82] m.l.c. in mg/litre		Contact Spray on *Aphis*,[83] % kill from 1% solution	
	2-Alkyl	4-Alkyl	2-Alkyl	4-Alkyl
Methyl	10.1	...	3	..
Ethyl	11.3	7.2	4	9
Propyl	4.8	3.5	7	14
Butyl	6.4	4.4	10	38
Amyl	10.8	8.0	34	80
Hexyl	Neg.	Neg.	69	99
Heptyl	Neg.	...	98	
Octyl	Neg.	...	97	

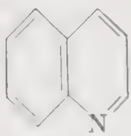
The toxicity of pyridine both as a fumigant and as a contact poison is increased by addition of alkyl groups to the carbon atoms in the ring (Table 16). Fumigant toxicity reaches a maximum at 4-propyl, while the highest contact toxicity develops at 4-hexyl- and 2-heptylpyridine. Whereas cuticular penetration is favoured by the longer aliphatic chain, the volatility and effectiveness of fumigants require a shorter chain length.

TABLE 17. Toxicity of Picolines, Lutidines, and Quinoline

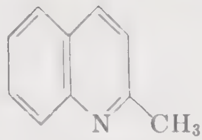
Chemical Compound	Fumigant on *Tribolium*,[82] m.l.c. in mg/litre	Contact Spray on *Aphis*,[83] % kill from 1% solution
Pyridine	7.2	2.4
α-Picoline (2-methyl)	10.1	2.9
β-Picoline (3-methyl)	5.4	8.4
2,4-Lutidine (2,4-dimethyl)	9.0	18.1
2,5-Lutidine (2,6-dimethyl)	6.6	20.5
2,6-Lutidine (2,6-dimethyl)	6.5	10.8
Quinoline	60.0	76.4

Substitution of a methyl group in the 3 position, to produce β-picoline, gives a more effective compound than 2-methylpyridine (α-picoline). Disubstitution of methyl groups induces a further increase in contact toxicity in the order pyridine < picoline < lutidine < quinoline (see Table 17).[186]

Ten-membered ring system. Quinoline, although less toxic than pyridine as a fumigant, is much more toxic as a contact poison and as an ovicide.[172] Derivatives of quinoline are less



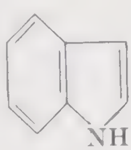
Quinoline



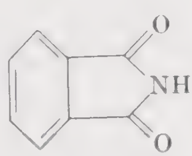
Quinaldine

insecticidal than the parent compound, although substitution of Cl, OH, or NO_2 in the 2, 6, or 8 position may increase the effectiveness against certain species.[178] The methylquinolines are in general slightly less active than quinoline, although quinaldine (2-methyl) shows a high degree of toxicity to *Cochliomyia* [15] and *Pediculus*.[16] Isoquinoline is also insecticidal to these species.

Nine-membered ring system. Indole has been found to be highly toxic to *Pediculus* and its eggs; [16] it is insecticidal to caterpillars but not to maggots.[15,183] Methylindole is also toxic to the body louse and the granary weevil. It is interesting that indole-acetic acid and -butyric acid, which are plant hormones, proved not to be insecticidal.[16]



Indole



Phthalimide

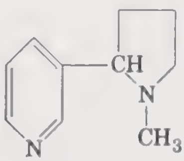
Phthalimide and its derivatives are ineffective, with the exception of butyl-tetrahydro-phthalimide, which was poisonous to lice. The N-substituted phthalimides, of which isopropylphthalimide was the most effective, were not very toxic to lepidopterous larvae.[5] The benzimidazoles, naphthimidazoles, and benzoxazoles showed no more than slight insecticidal activity.[43,168,183]

Purines and hydantoins have not proved to be insect poisons; neither have the derivatives of barbituric acid, quinoxaline, and piperazine that have been tested. Alkaloids such as strychnine, atropine, brucine, quinine, and pilocarpine showed no contact toxicity to insects.[111] However, eserine was almost as effective

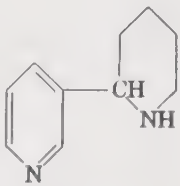
as nicotine against *Aphis*,[186] and cinchonine proved highly insecticidal to *Cochliomyia*.[15]

Nicotine and anabasine

Combination of the pyridine ring with the pyrrolidine or piperidine ring results in alkaloids of pronounced pharmacological activity. Nicotine is found in the plant *Nicotiana* as *l*-β-pyridyl-α-N-methylpyrrolidine, while anabasine is found in the plant *Anabasis* as *l*-β-pyridyl-α-piperidine. Both compounds exhibit linkage from the β (or 3) position in pyridine to the asymmetrical α-carbon of pyrrolidine or piperidine.



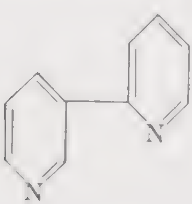
l-β-Nicotine



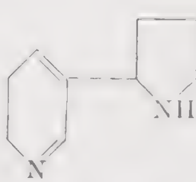
Anabasine

A full series of investigations has yielded material for the study of comparative toxicity of compounds in this group. The dipyridyls are considerably toxic to insects, and the saturated dipiperidyls even more so. Of the five forms of linkage possible (α,α, β,β, γ,γ, β,γ, α,γ) the most toxic was the α,β-dipyridyl.[144]

The pyridyl-piperidines were even more poisonous. Here again the β,α (α,β) isomer was much more toxic than the α,α, β,β (nicotidine), or γ,γ (isonicotine) structural isomer.[173] This β,α compound was called neonicotine, and being of synthetic origin was a racemic mixture of its two optical isomers. It was found that anabasine was the laevorotatory component of neonicotine, and accounted for the greater part of its toxicity. Anabasine is more toxic to *Aphis rumicis* than is *l*-nicotine.[142]



α,β-Dipyridyl



β-Nornicotine
(*β-Pyridyl-α-pyrrolidine*)

With the pyridyl-pyrrolidines the β,α is again the most toxic structural isomer and is termed β-nornicotine. The same relation holds if the pyrrolidine is N-methylated, where the β,α isomer (which is β-nicotine) is 30 times as toxic as the α,α isomer (α-nicotine), as was found with the nornicotines. The nicotines are equitoxic with the nornicotines, the N-methyl group having no effect on the contact insecticidal action. However, with vertebrates the nicotines are more toxic to some species than the nornicotines, and less toxic to others; although in all cases the β,α isomers are more toxic than the α,α nicotines and nornicotines.

Further changes in the nicotine molecule do not increase toxicity, but decrease it. Saturation of the pyrrolidine ring produces β-pyridyl-α-N-methylpyrrole, also called nicotyrine, which shows one-tenth the contact toxicity of β-nicotine. Partial saturation to produce dihydronicotyrine, the pyrroline analogue, produces a compound which proves to be 3 times as toxic as nicotine on injection into *Oncopeltus*. Desaturation of the pyridine ring produces piperidyl-N-methylpyrrolidine or hexahydronicotine, which shows one-hundredth the toxicity of nicotine.[145] Opening the linkage between the α-carbon and the nitrogen of the pyrrolidine ring produces metanicotine, with one-tenth the toxicity of nicotine. Compounds with the pyrrolidine ring broken at other points were less than one-hundredth as toxic as nicotine.[145]

It is evident that the more important factor in the toxicity of the nicotine molecule is the pyrrolidine ring, since pyrrolidine is a considerably more toxic fumigant and contact poison than pyridine.[27,145] If substitution is made on the 3-carbon of pyrrolidine, compounds with contact toxicity may be made with other aromatic substituents, increasing in effectiveness from phenyl < thienyl < cyclohexyl < 2-mesityl-α pyrrolidine, the last derivative showing one-third the toxicity of nicotine. Similar derivatives of pyrroline (dihydropyrrolidine) are on the whole slightly more toxic than the pyrrolidines.[84] The aromatic derivatives of pyridine also are most toxic when substituted at the α position (e.g. benzyl-α-pyridine).[145]

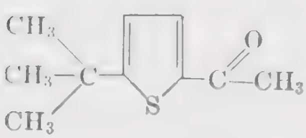
Thus, not only the most toxic of the dipyridyls, but also anabasine, nicotine, and nornicotine, show the substitution of β-pyridine on the α-carbon of the nitrogenous ring. In the last three compounds, all highly toxic, this α-carbon is asymmetrical and

is considered to be the significant point in their toxicity. Curiously enough, both steric isomers of β-nornicotine are equitoxic,[62] as also are the two enantiomorphs of cyclohexyl-α-pyrrolidine.[64] However, with β-nicotine the naturally occurring *l* isomer shows ten times the contact toxicity to *Aphis* that the *d* isomer does, but *Drosophila* larvae are equally susceptible to the two optical ismers.[62]

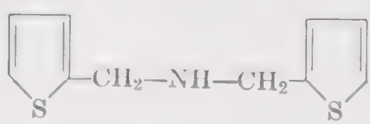
The nicotinium salts, which are quaternary compounds in which alkyl halides are added to one or both of the tertiary amines of nicotine, are in general of lesser toxicity. Only one nicotinium compound was more toxic than nicotine to *Aphis rumicis*, and only three to *Prodenia* larvae, whereas sixteen were more toxic than nicotine to *Diaphania* larvae. Five compounds were more toxic than nicotine on injection into *Oncopeltus*. In general, the N-dodecylnicotinium kation is most effective, followed by the methylnicotinium kation.[194]

Heterocyclic compounds with S in the ring

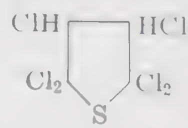
Thiophene is non-toxic to insects.[43] The substitution of 2,5-dichlorothienyl for the *p*-chlorophenyl radicals in the DDT molecule results in a reduction of the toxicity to most insect species, although the symptomatology is unchanged.[12, 115] None of the five dithienyltrichloroethanes tested against *Drosophila* and *Heliothrips* showed contact toxicity comparable to DDT derivatives, although they were dehydrohalogenated in alkali just as readily as the corresponding DDT derivatives.[116] The chlorinated dihydro and tetrahydro thiophenes were found to show



5-*t*-Butyl-2-acetylthiophene

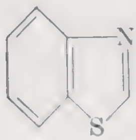


Di-2-thenylamine

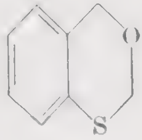


Tetrahydrohexachlorothiophene

considerable toxicity to *Sitophilus*. This species was also susceptible to 3-thiophenethiol and its allyl and benzyl sulfides. Whereas 2-thenylamine is slightly toxic, di-2-thenylamine shows a direct contact toxicity to *Blattella* only slightly inferior to that of DDT. Good contact toxicity is shown by 2-acetylthiophene, which is improved in its 3-methyl and 5-*tert*-butyl derivatives.[234]



Benzothiazole



Benzoxathian

Of the derivatives of thionaphthene (benzothiophene) tested, none have proved to be more than slightly toxic.[183] Similar ineffectiveness characterizes the thiazoles, which contain N and S in a five-membered ring.[43,180] However, an alkyl 2-thiazolinyl sulphide has proved a highly effective acaricide against orchard mites, although it is not insecticidal.[23] Many derivatives of benzothiazole have been tested, and most are of negligible toxicity.[183] However, the 1-methyl derivative is lousicidal, 1-phenylbenzothiazole is larvicidal to *Culex*, and the 2-thiocyano derivative is toxic to houseflies, aphids, and the carpet beetle.[22,40] Of the few analogues of benzoxathian that have been tested, the 2-methyl-4-oxo derivative shows high toxicity to *Sitophilus* and *Blattella*. There is evidence that the dithianes and thioxanes are insecticidal but without contact activity.

Diphenyl sulphides, sulphoxides, sulphones, and sulpho esters

It was observed by Läuger, Martin, and Müller that the most toxic of the diphenyl sulpho esters, sulphides, sulphoxides, and sulphones, diphenyl ethers, and phenyl benzyl ethers were those in which the benzene rings were halogenated in the *p,p′* position. Other workers using other insect species have confirmed their findings. These researches, although first concerned with stomach insecticides for the clothes moth, led to the discovery of the contact insecticide *p,p′*-dichlorodiphenyltrichloroethane, or DDT.[89]

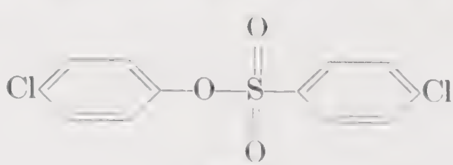
Sulphides. Whereas diphenyl sulphide (ϕ-S-ϕ) and dibenzyl sulphide are only slightly toxic, *p,p′*-dichlorodiphenyl sulphide is a highly effective stomach poison for *Tinea*[89] and is highly larvicidal to *Anopheles*.[34] However, it proves to be a poor contact poison to *Epilachna*, *Oncopeltus*, and *Musca*. The *p,p′*-dinitro, -dimethyl, and -diamino analogues were non-toxic.[72,183] The diamino analogue is highly bactericidal, and it was noted that if the free amino group of an effective sulphonamide were replaced by chlorine, an effective insecticide would result.[89]

Sulphoxides. Diphenyl sulphoxide (ϕ-SO-ϕ) is six times as toxic as the sulphide.[15] However, the *p,p′*-dichlorodiphenyl sulphoxide shows only one-hundredth the toxicity of the analogous sulphide.[34]

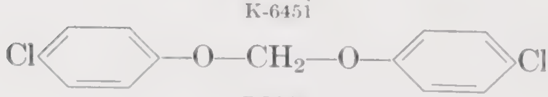
Sulphones. Diphenyl sulphone (ϕ-SO_2-ϕ) is virtually nontoxic. The *p,p′*-dichloro derivative is a good mosquito larvicide but is valueless as a contact application or residual deposit. The dibromo analogue shows no toxicity.[13, 183] Further addition of chlorine to *p,p′*-dichlorodiphenyl sulphone reduces the toxicity, and removal of one or both *p*-Cl atoms eliminates it entirely.[89] Both the *p,p′*-dimethyl and -dimethoxy derivatives are without insecticidal activity.[89, 183]

Disulphides and disulphoxides. Diphenyl disulphide (ϕ-S—S-ϕ) is slightly toxic, and di-*p*-tolyl disulphide a little more so. The derivatives tested, which did not include the *p,p′*-dichloro, showed little toxicity, with the exception of *p,p′*-difluorodiphenyl disulphide, which was an effective lousicide and mosquito larvicide. *p,p′*-Dichlorodiphenyl disulphoxide was slightly toxic to *Musca* and *Prodenia.*

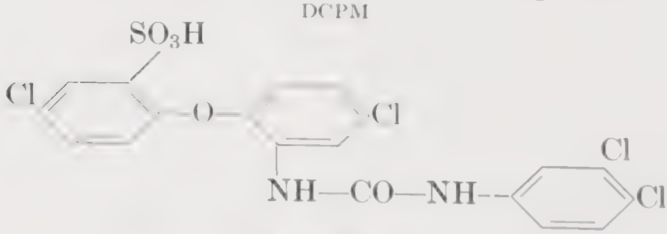
Sulpho esters. Out of a long series of 31 chlorinated phenyl esters of benzenesulphonic acid (ϕ-SO_2-O-ϕ) that have been tested, only the *p,p′*-dichloro sulpho ester showed high toxicity to clothes-moth larvae.[89] However, it has been found that both phenyl and *p*-chlorophenyl benzenesulphonate were more toxic to codling moth than lead arsenate. The *p*-chlorophenyl-*p*-



K-6451



DCPM



Mitin FF

chlorobenzenesulphonate, already mentioned, has proved to be an acaricide of outstanding residual effectiveness, and is known as K-6451. Other sulpho esters, including *p*-tolyl *p*-toluenesulphonate, are of negligible toxicity.[165]

Phenyl benzenesulphonamides. In view of the bactericidal potency of *p*-aminobenzenesulphonamide (termed sulphanilamide), a great number of N-phenyl benzenesulphonamides (benzenesulphonanilides) were tested as insect poisons. None, including the 4,4′-dichloro derivative, proved to show any toxicity.[162, 167, 183] However, the 3,4,3′,4′-tetrachloro derivative, although not particularly toxic to clothes moths, was an outstanding poison for *Leptinotarsa*.[89]

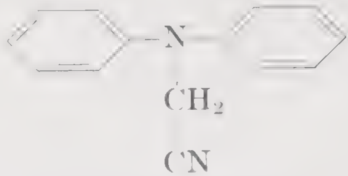
Diphenyl ethers. Diphenyl ether is of slight toxicity, which is not enhanced by the addition of nitro groups.[15] However, *p,p′*-dichlorodiphenyl ether (Cl-ϕ-O-ϕ-Cl) and *p*-chlorophenyl *p′*-chlorobenzyl ethers are effective stomach poisons for insects,[89] and the latter is highly acaricidal.[113] The di-ether analogue, di-4-chlorophenoxymethane (DCPM), is an excellent acaricide. However, di(*p*-chlorophenoxy)ethane was scarcely acaricidal at all.[113] The ω-methylated *p,p′*-dichlorodibenzyl ether is a good insecticide and mothproofing agent.[126] Combination of the insecticidal *p,p′*-dichlorodiphenyl ether grouping with a urea radical, which promotes its cotton-impregnating power, resulted in the moth-proofing compound *Mitin FF*.[89]

Diphenylamines and other nitrogenous groups

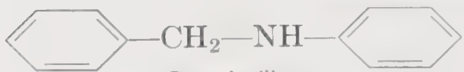
Diphenylamine itself is a moderately good insecticide and acaricide, is one of the most effective agents for protecting myiasis of wounds, and has been used as a lousicide in Russia. The *p,p′*-dichloro derivative shows limited residual toxicity to *Drosophila*. Whereas 2,4,4′-trinitrodiphenylamine is effective as a codling-moth poison,[164] the 2,4,6,2′,4′,6′-hexanitro derivative is a moderately good contact dust for caterpillars.[183] A full series of derivatives with OH, NH_2, SCN, CH_3, and acetyl substitution was found to show negligible toxicity. Addition of a nitroso group to the imino nitrogen of diphenylamine produces an acaricidal clothing impregnant, which is also moderately insecticidal; however, the derivatives of N-nitrosodiphenylamine are not toxic.[183] Other N-substituted diphenylamines are ineffec-

tive, with the exception of N-diphenylglycinonitrile, which is highly toxic to *Aphis rumicis*.[122]

Diphenylamine



N-Diphenylglycinonitrile



Benzylaniline

N,N-Benzylphenylglycinonitrile is also highly toxic to *Aphis*, but other derivatives of benzylaniline, including the N-nitroso, are of low or negligible toxicity. Although the unsaturated benzalaniline (ϕ-CH=N-ϕ) is moderately poisonous to caterpillars, its derivatives are ineffective.[183] Benzanilide and its derivatives are not insecticidal. Dibenzylamine (ϕ-CH_2-NH-CH_2-ϕ) is slightly toxic, its N-nitroso derivatives more so, and dibenzylglycinonitrile is more effective than the diphenyl analogue.

TABLE 18. TOXICITY OF AROMATIC AMINES TO *Aphis rumicis*[186]

Values of LC_{90} in moles/100 cc of contact spray

Aniline	0.053–0.10	Benzylamine	0.019
Diphenylamine	0.003	Dibenzylamine	0.0025
Triphenylamine	0.004	Tribenzylamine	0.007

Other diphenyl compounds linked by C and N, including diphenyl and dibenzyl ureas, thioureas, and guanidines, are of negligible toxicity.[13] The tertiary amines, triphenylamine and tribenzylamine, and the di-2ndary amine, N,N-diphenyl-*p*-phenylenediamine, are virtually inactive. The increase in toxicity that occurs in passing from the primary amine to the secondary, and decreasing again to the tertiary, is shown in Table 18.

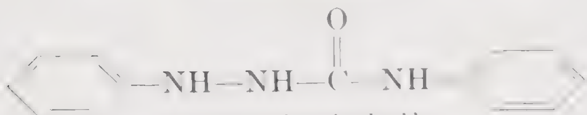
Phenylazo compounds

Whereas hydrazobenzene is moderately toxic, azobenzene is strongly insecticidal and acaricidal.[184] The halogenated azobenzenes are of mediocre toxicity, and the other derivatives are ineffective. However, *p*-aminoazobenzene (*p*-phenylazoaniline)

and its hydrochloride are strongly insecticidal.[179] Azoxybenzene is also considerably toxic, but its *p,p'*-dichloro and -diiodo derivatives are ineffective.[15,183] Diazoaminobenzene (1,3-diphenyltria-

p-Aminoazobenzene

Diazoaminobenzene



1,4-Diphenyl semicarbazide

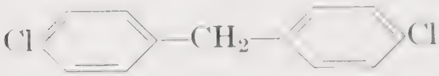
zene) and benzeneazodiphenylamine (*p*-phenylazodiphenylamine) show moderate toxicity; *p*-(phenylazo)-azobenzene is nontoxic.[183] 1,4-Diphenyl semicarbazide is more poisonous to caterpillars and other insects than is derris dust.[17] However, its derivatives, including the thiosemicarbazide, are of negligible toxicity.[182] N-(phenyldiazo)-piperidine has been used in Germany as a roach poison under the name of *Dizan*, and as a dust against forest defoliators under the name of *Nemotan*.

Derivatives of diphenylmethane

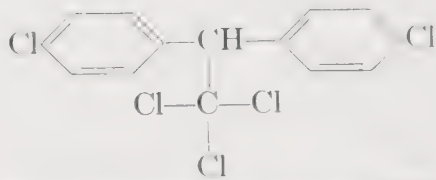
Diphenylmethane has slight to moderate insecticidal value, and most of its derivatives show no more than slight toxicity. Whereas halogenation of the methane nucleus is ineffective, substitution of halogens on the benzene rings greatly increases the toxicity. The *p,p'*-dichloro-, *p,p'*-dibromo-, and *o,p'*-dichlorodiphenylmethanes have been found to be larvicidal to *Anopheles* at dosages as low as 1 ppm.[34]

Benzohydrol is inactive, but its *p,p'*-dichloro derivative is moderately toxic.[13] Benzophenone is a fairly good mosquito larvicide, lousicide, and acaricide, but it is ineffective against caterpillars. An incense containing benzophenone has been found to be highly effective against adult mosquitoes.[175a] The only derivatives which were found to be toxic were chlorinated compounds such as *p*-chloro- and *p,p'*-dichlorobenzophenone, which were larvicidal to *Anopheles* at 10 ppm. The *o*-chlorinated ben-

zophenones proved to be good stomach poisons for *Tineola*. On the other hand, *p,p'*-dichlorodiphenylmethane and -benzophenone, though toxic to other chewing insects, were not effective as stomach poisons to the clothes moth.[89]



p,p'-Dichlorodiphenylmethane



p,p'-Dichlorodiphenyltrichloroethane (DDT)

Diphenylethane (1,1-) is as toxic as diphenylmethane.[34] Halogenation to produce *p,p'*-dichlorodiphenylethane results in a great increase in insecticidal power.[18] Further chlorination on the 2 position of the ethane nucleus results in *p,p'*-dichlorodiphenyltrichloroethane. This compound, known as DDT, not only possesses a high toxicity but also is extremely stable and non-volatile, and has a remarkable contact affinity for insect cuticle. These three qualities make it the most generally effective synthetic insecticide yet discovered. DDT may be regarded as the climax of a course of synthesis which led through the *p,p'*-dichlorodiphenyl sulphides, sulphoxides, sulphones, and sulpho esters to dichlorodiphenylmethane and -ethane, and finally to *p,p'*-dichlorodiphenyltrichloroethane.[89]

Toxicity of analogues of DDT

Since the discovery of the insecticidal power of DDT, an extensive series of researches has been centred on other compounds built on a framework of 1,1-diphenylethane. So far only three of these analogues have been found to rival DDT. However, the instances in which they are superior are outnumbered by the cases in which they are found to be less insecticidal than DDT. The analogues concerned are:

Difluorodiphenyltrichloroethane, termed *Gix*, fluoro-DDT, or DFDT.

Dimethoxydiphenyltrichloroethane, termed methoxy-DDT or methoxychlor.

Dichlorodiphenyldichloroethane, termed DDD or TDE.

The points at which the DDT molecule may be modified to produce new compounds, and the trends in synthesis of new analogues, are as follows:

1. Alteration of the positions of the chlorine atoms on the benzene rings to produce structural isomers of DDT.
2. Replacement of the chlorine atoms with other halogens.
3. Substitution of other radicals on the benzene rings.
4. Subtraction, or addition, of chlorine atoms on the trichloroethane location in the molecule.

Compounds developed along these lines of synthesis are shown in Tables 19 and 20, in which their insecticidal activity has been indicated.

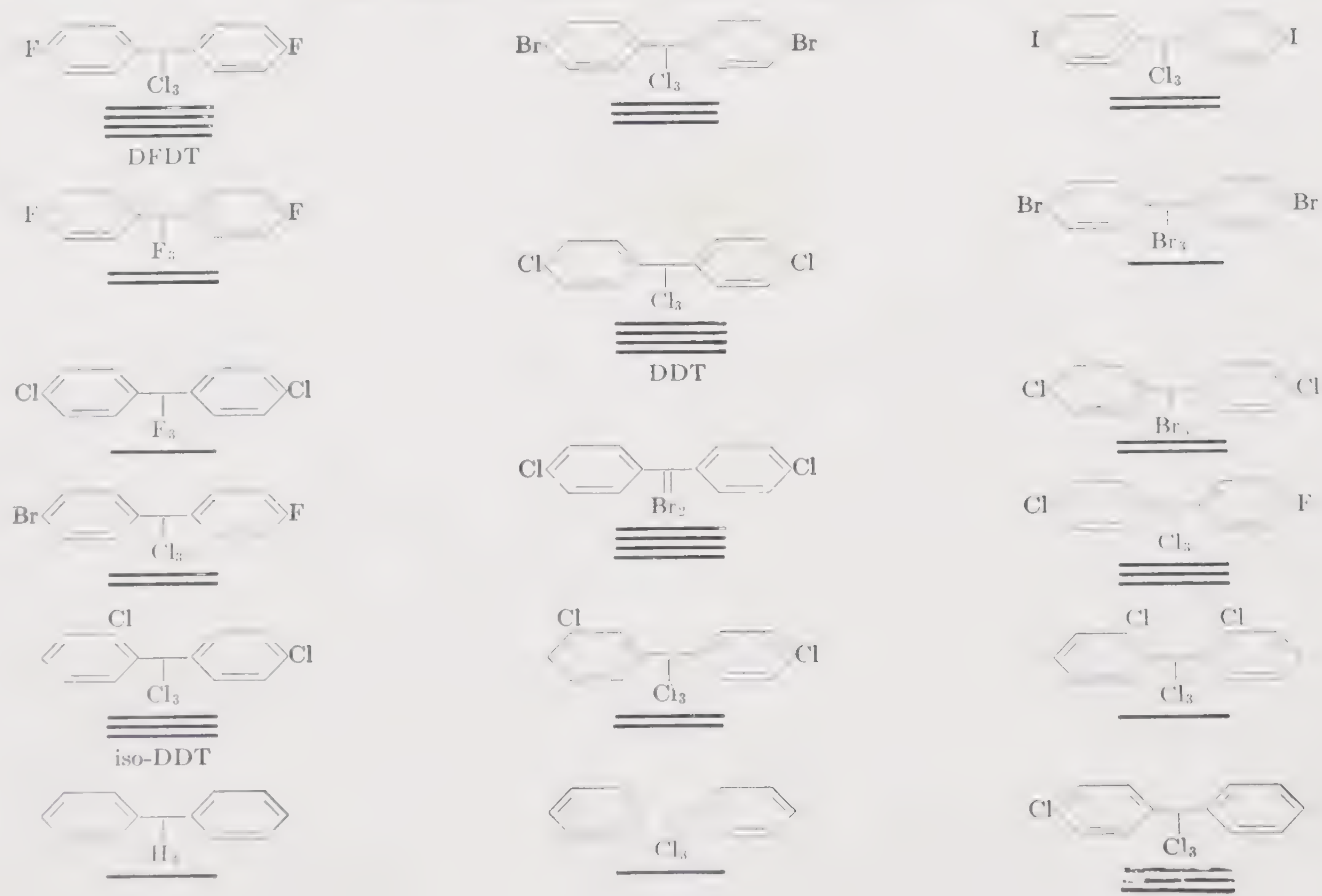
1. Structural isomers of DDT. Tests performed on *Pediculus* and adults of *Musca* and *Anopheles* have shown that the order of toxicity of the isomers is $p,p' > o,p' > o,o'$.[28] The following minimum lethal concentrations were obtained for *Anopheles* larvae: *p,p'*, 0.0025; *m,p'*, 0.005; *o,p'*, 0.025 ppm.[34]

When one of the chlorine atoms is removed from one of the benzene rings, as in 1-(*p*-chlorophenyl)-1-phenyltrichloroethane, the resulting compound is intermediate between the *m,p'* and *o,p'* isomers in its toxicity.[13, 19, 34] Diphenyltrichloroethane, in which both chlorine atoms are removed, is moderately larvicidal for mosquitoes[34, 129] but otherwise shows negligible insecticidal activity.[12, 106, 141]

2. Substitution of other halogens. Chlorine may be replaced by fluorine, bromine, or iodine in the *p,p'* position on the benzene ring. Tests performed on several species of insects in Europe, and assessment of residual toxicity to *Drosophila*, originally represented the order of toxicity to be fluoro- > chloro- > bromo- > iodo-DDT.[13, 89] More detailed investigation in Britain and America showed that to 16 out of 21 species of insects fluoro-DDT was not as toxic as DDT.[6, 21, 114, 129] Fluoro-DDT, now called DFDT, was more toxic than DDT to *Blattella*, *Oncopeltus*, and *Tribolium*, which are comparatively resistant to DDT poisoning.[13, 114] As a larvicide for *Anopheles* DFDT was less toxic than either bromo-DDT or DDT.[34] Its toxicity to goldfish and *Gambusia* is least of all the halogenated analogues of DDT, a property that may make it desirable for treatment of natural

TABLE 19. TOXICITY OF DDT ANALOGUES: SUBSTITUTION OF OTHER HALOGENS, AND STRUCTURAL ISOMERS

The number of underlines indicates the degree of toxicity



waters.[129] Moreover the speed of insecticidal action of fluoro-DDT is much greater than that of DDT.[111] Bromo-DDT is less toxic than DDT on a weight basis but equitoxic on a molar basis; iodo-DDT is definitely the least effective, even on a molar basis.[176]

If the three chlorine atoms of the ethane radical of DDT are replaced with fluorine or with bromine, the resulting compounds are slightly or moderately toxic respectively. If all five chlorine atoms are replaced with fluorine or bromine, the resulting compounds are, respectively, of moderate or of light toxicity. Replacement of one of the two *p*-chloro substituents by fluorine results in a reduction of toxicity, although the compound is still highly insecticidal. Substitution of dibromomethylene for trichloroethane yields a compound whose residual toxicity to houseflies is the equal of DDT.

3. Other substituents on the benzene rings. Replacement of the two *p*-chloro groups by methyl groups gives a compound of moderate to high toxicity. Methyl-DDT has shown excellent results against *Carpocapsa*,[163] and tests have shown it to be moderately toxic to five species[18,34] and slightly toxic to seven species.[11,13,89,141] Ethyl-DDT, with a longer side-chain, is more toxic than the methyl analogue to some species and less toxic to others.[19] Further increase in the side-chain, e.g. *tert*-butyl-DDT, results in a great decrease of toxicity.[34] Addition of further methyl groups to methyl-DDT in the *m*,*m*′ position results in sporadic toxicity.[38] Addition of methyl groups to DDT itself, in the *m*,*m*′ or the 3,5,3′,5′ position, gives scarcely active compounds.[19,89]

Replacement of the two *p*-chloro groups by methoxy groups yields a compound that in some cases is more toxic than DDT. Methoxy-DDT (methoxychlor) gives better knockdown of houseflies[139] and is highly effective against codling-moth larvae.[163] Moreover it is less toxic to mammals than DDT. As a mosquito larvicide, it is equitoxic with DDT against *Culex*[139] but less toxic to *Anopheles*,[34] while being just as poisonous to fish.[52] It has proved to be less toxic than DDT to five out of six species of insects tested. Addition of chlorine or bromine to the phenyl groups of methoxychlor greatly reduces the toxicity.[17,34] Doubling the methoxy substitution to give a 3,4,3′,4′- or 2,5,2′,5′-

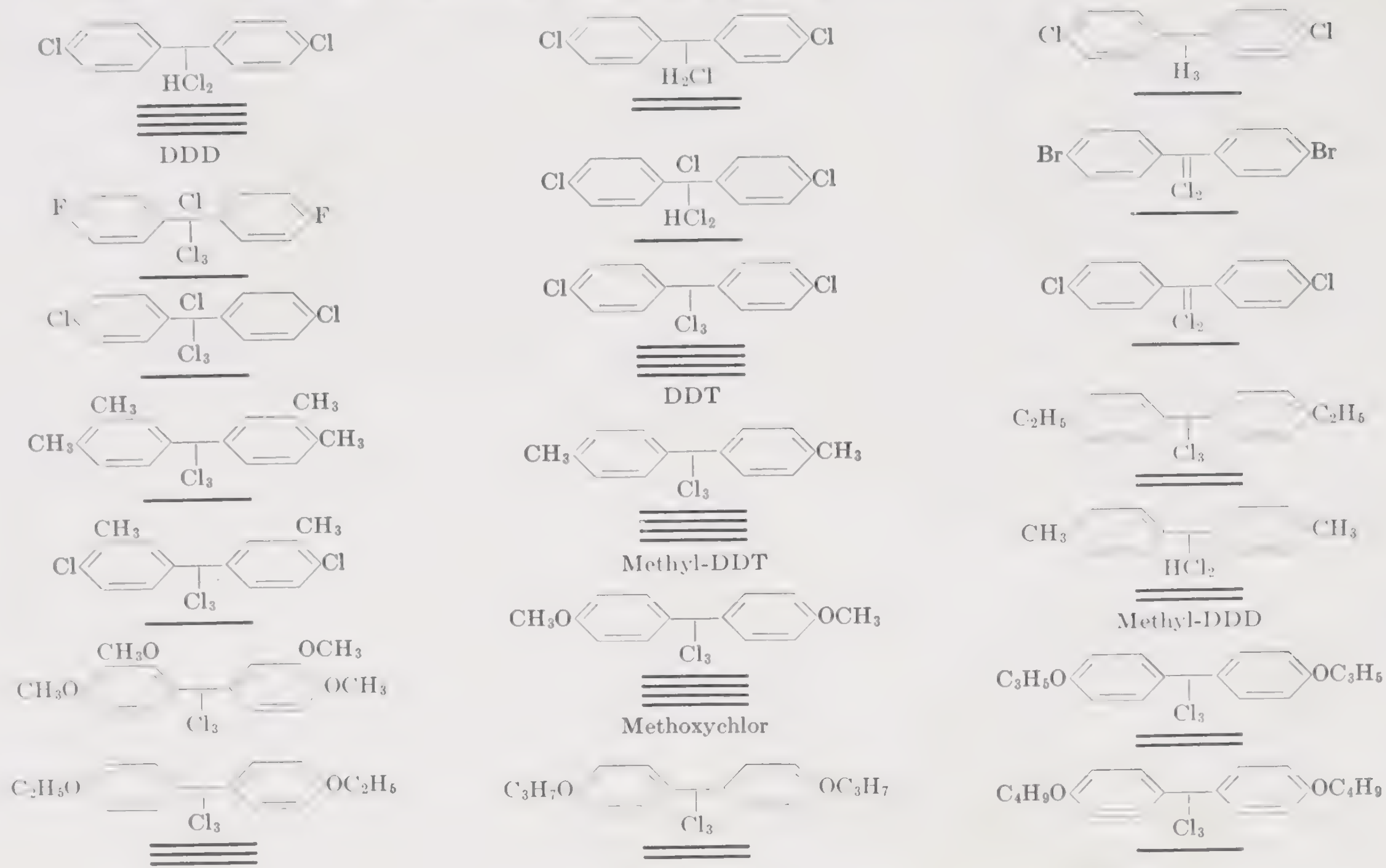
tetramethoxy analogue results in the elimination of toxicity.[19,34] Ethoxy-DDT has a toxicity against *Musca* adults and *Culex* larvae equally as high as that of methoxychlor.[139] However, it has proved to be less effective than methoxychlor to five out of six species tested. Higher in the series, the propoxy and alloxy analogues are only one-tenth as toxic as their predecessors,[17,139] and butoxy-DDT is even less toxic.[140]

Replacement of the *p*-chloro groups of DDT with hydroxy groups results in a non-toxic compound.[34,89,106] All analogues bearing the highly polar OH groups on the benzene ring are found to show negligible contact toxicity. Addition of nitro groups to DDT in the *m,m'* position or the 3,5,3',5' position yields ineffective compounds.[17,34,89] It has been the experience that addition of any substituent to the intact DDT molecule results in a loss of toxicity.[17]

4. Subtraction of chlorine from the ethane group. Tests for insecticidal activity have all shown that toxicity progressively decreases as chlorine is subtracted from the 2-carbon of the ethane nucleus of DDT.[176] The order of toxicity can therefore be represented as follows: CCl_3 (in DDT) $>$ $CHCl_2$ (in DDD) $>$ CH_2Cl $>$ CH_3. However, DDD (dichlorodiphenyldichloroethane) is as good a larvicide as DDT for *Anopheles*,[34] and it is less toxic to fish;[32] curiously enough, *o,p'*-DDD is also equitoxic with *o,p'*-DDT for *Anopheles*. DDD has proved to be less toxic than DDT to the nine other species of insects on which tests have been carried out.[18,123,126,141] The fluorine analogue, DFDD, is correspondingly less toxic than DFDT.[141] Similarly, subtraction of one chlorine atom to give the dichloroethane analogue, from either methyl-DDT or methoxychlor, has the effect of reducing the toxicity slightly. The monochloroethane analogue of DDT is of moderate toxicity,[126] while the analogue which lacks any chlorine on the ethane nucleus is only slightly toxic. All the derivatives of the last-named analogue have been found to be negligibly insecticidal.[34]

If DDT is submitted to dehydrohalogenation, the result is dichlorodiphenyldichloroethylene, in which $C{=}CCl_2$ replaces the ethane nucleus. This compound has shown a consistently low degree of toxicity against many insects.[11] Of all the DDT analogues which have a trichloroethane nucleus, the dichloro-

TABLE 20. TOXICITY OF DDT ANALOGUES: THE EFFECT OF REMOVING CHLORINE FROM THE ETHANE NUCLEUS AND SUBSTITUTING OTHER GROUPS ON THE BENZENE RINGS

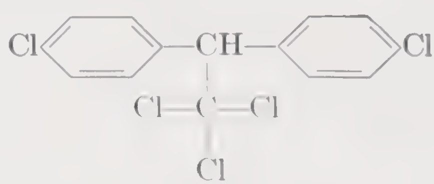


ethylene derivatives arising from them by dehydrohalogenation are less toxic than the parent compound.[123]

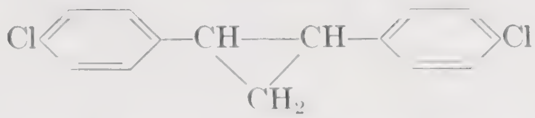
If, instead of subtracting chlorine from DDT, a fourth chlorine is added to the trichloroethane nucleus in the 1-carbon position, the result is a relatively ineffective compound.[12, 31, 89] The tetrachloroethane derivatives of DFDT and of methyl-DDT are also negligibly insecticidal.

Molecular structure of DDT analogues and their toxicity

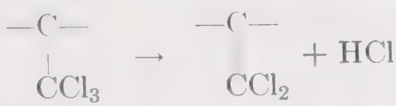
Mention has already been made of the discovery that substitution of chlorine in the *p,p′* position on diphenyl sulphoxides, sulphides, sulphones, and sulpho esters makes for highly insecticidal molecules. Substitution of the sulphoxide group by a trichloroethyl group, which is also strongly electronegative, confers lipoid solubility on the resulting molecule of DDT. Thus the symmetrical apolar molecule of DDT is capable of showing toxic action by mere contact with the lipoid epicuticle of insects. The high contact toxicity of DDT may be related to its molecular structure in that it is composed of a toxic fumigant poison combined with a lipoid-soluble narcotic.[89] The molecule of DDT may be regarded as methane substituted with two chlorobenzene groups and a chloroform group:



Chlorobenzene is toxic to insects, and addition of a second chlorine in the *para* position produces the highly toxic fumigant *p*-dichlorobenzene. This group may therefore be regarded as a toxophore in the sense of Ehrlich. Chloroform is a strong narcotic and is soluble not only in the lipoids of nerve sheaths but also in the waxy epicuticle of insects. Combination of 2 moles of chlorobenzene with 1 mole of other narcotics, such as bromoform, methylene chloride, nitromethane, ethylene, diethyl ether, and divinyl ether, also produced good contact insecticides, and condensation with the anaesthetic cyclopropane resulted in a contact insecticide of outstanding effectiveness.[89]



On the other hand it has been suggested that it is the chlorobenzene group which confers lipoid solubility and the remainder of the molecule is responsible for the toxicity.[107] In methoxychlor it is the methoxybenzene portion of the molecule which is lipoid-soluble, whereas methoxybenzene (anisole) is not toxic to insects. It is further suggested that the toxicity is related to the release of toxic HCl in the insect tissues, since DDT is highly susceptible to dehydrohalogenation by mild alkali.



Careful examination has been made of the relation between dehydrohalogenation and toxicity in DDT and a large number of its analogues. There is undoubtedly a general correlation, especially if the analogues are considered in three groups[123] (Fig. 10). The compounds in class 1, which readily split off HCl in the presence of alcoholic KOH, include DDT, DFDT, and DDD. Class 3, characterized by comparative resistance to dehydrohalogenation, contains fourteen compounds (including dichlorodiphenyltetrachloroethane) none of which show any more than the slightest toxicity. The intermediate class contains six compounds of moderate toxicity, and in addition methoxychlor, methyl-DDT, and methyl-DDD, which are more toxic than their susceptibility to dehydrohalogenation would appear to warrant. However, diphenyldichloroethane (DD) is non-toxic, in spite of being more than twice as susceptible to dehydrohalogenation as its *p*-dimethyl analogue, methyl-DDD. The susceptibility of the isomers of DDT to dehydrohalogenation follows their order of toxicity:

$$p,p', \ 0.99\%; \quad m,p', \ 0.87\%; \quad o,p', \ 0.10\%; \quad o,o', \ 0.0\%$$

A similar correlation is evident in the halogenated analogues—fluoro > chloro > bromo— in both the DDT and DDD series.

All the dichloroethylene derivatives are less toxic than the parent trichloroethane analogues: this could be interpreted to indicate that they have no toxic HCl to liberate in the tissues by dehydrohalogenation of the ethane nucleus.

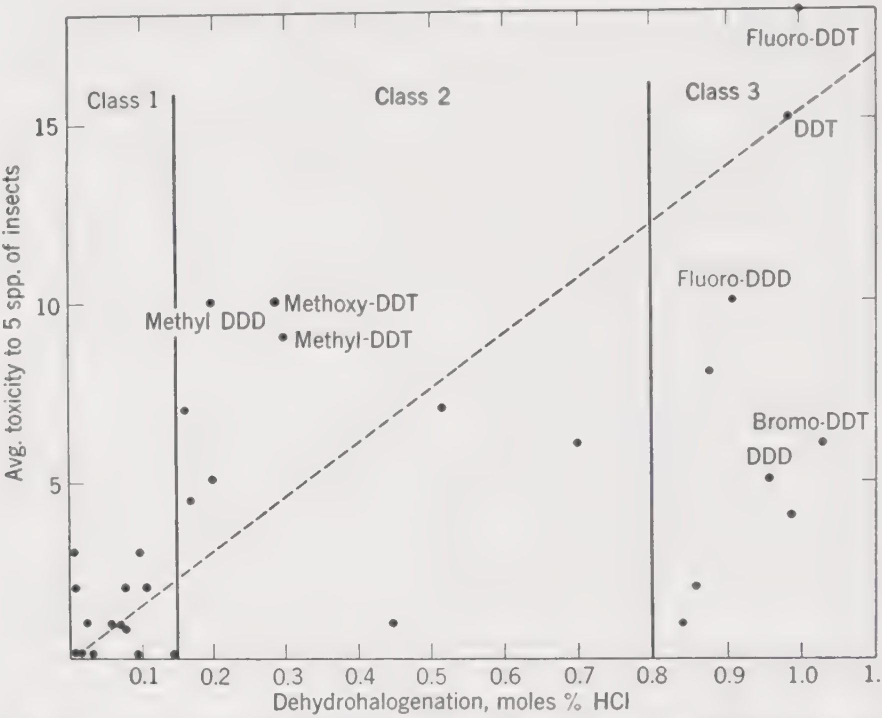


FIG. 10. Susceptibility of DDT analogues to dehydrohalogenation, and its relation to their toxicity to five species of insects. (From Müller)

When the question of lipoid solubility is examined, it is found to bear no direct relationship to contact toxicity (Table 21). Although DDT is appreciably liposoluble, most of its analogues, including the non-toxic ones, are considerably more so.[18, 38] However, it may well be that nearly all the DDT analogues are above the threshold liposolubility necessary, only dichlorodiphenylacetic acid (DDA), which is quite lipoid-insoluble, being below the threshold necessary for contact action. On the other hand the highly liposoluble analogues may owe their lack of toxicity to a water lipoid partition coefficient so low that they cannot enter the aqueous phase of the insect's body fluids.[202]

TABLE 21. LIPOSOLUBILITY AND TOXICITY OF DDT ANALOGUES[15]

Compound	Toxicity, m.l.c.		Hydrolysis, 1% hydrolysed after 240 min	Solubility, wt./vol. % at 18° C	
	Pediculus	*Cimex*		Olive Oil	White Oil
DDT (*p,p'*)	0.3	0.53	100	10	2–3
Methoxychlor	0.9	0.55	10	8–10	1–2
DDD	0.9	1.2	33	10	1–2
Methyl-DDT	1.7	3.6	8	18–20	6–8
iso-DDT (*o,p'*)	5.5	20	13	25	10–14
Diphenyltrichloroethane	7.5	20	10	25–30	10–12
Dichlorodiphenyl ethane	8.5	20	..	20	25
Dichlorodiphenyl-dichloroethylene	20	20	..	14–18	8–10

It may be concluded that although there is general relationship of toxicity with (i) the *p*-chlorophenyl group, (ii) the lipoid-soluble or narcotic nucleus of trichloroethane, (iii) solubility in lipoids, and (iv) susceptibility to dehydrohalogenation, the following important exceptions can be found in each case:

(i) Methyl-DDT and methoxychlor are highly toxic.

(ii) There are analogues lacking the trichloroethane nucleus which are no less toxic than DDT (e.g. DDD to *Anopheles*) and are more lipoid-soluble than DDT (e.g. dichlorodiphenyl-dichloroethylene).

(iii) The relation of toxicity with lipoid solubility is erratic. and more inverse than direct.

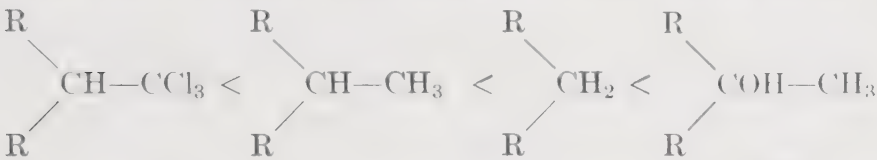
(iv) Methoxychlor, methyl-DDT, and methyl-DDD are comparatively resistant to dehydrohalogenation.

Thus any attempt to obtain any complete quantitative correlation with any single property ends in failure, which is perhaps not surprising in view of the factors involved in the process of poisoning by contact. Perhaps greater success may be obtained by considering the shape of the molecule. In this regard it may be observed that the most effective molecules—DDT, DFDT, methoxychlor, methyl-DDT, DDD, and the cyclopropane analogue—

are all symmetrical. All these compounds have substituents in the *p,p'* position, and subtraction of one of them, or addition of any further substituents, will detract from the toxicity. If the length of side-chains is increased, the toxicity decreases.[140] As far as toxicity to mammals is concerned, only those compounds halogenated in both the phenyl and ethane components show the characteristic neurotoxic symptoms.[175] The most recent view is that the spatial relationship of the different parts of the DDT molecule to each other is the most important factor. It is suggestive that *p*-chlorophenylhexachloropropane, which has two chloroform groups to one *p*-chlorophenyl group, shows a residual toxicity equal to that of DDT, with one chloroform to two chlorophenyl groups. Yet when the chlorine atoms of DDT are replaced with CH_3 or OH groups, which have a similar spatial configuration, the insecticidal activity is almost entirely lost.[170a]

Nearly all the DDT analogues that have been investigated have caused similar physiological symptoms, involving the nervous system of animals.[38, 200] The effect on isolated nerve is reversible provided the molecular density of the poison is not too great. Increasing halogenation of the molecule increases its density, so that the effect with bromo-DDT becomes scarcely reversible; with DDT, DFDT, and methoxychlor slowly reversible; with DDD and dibenzylethane quickly reversible; and with diphenylethane very quickly reversible. It has been suggested that the high molecular density makes the drug "stick" to the receptor it blocks. DDA and *p,p'*-dihydroxydiphenyltrichloroethane, which carry the highly polar COOH and OH groups, cause transitory symptoms differing from those due to DDT. The DDT effects may be regained in the case of the dihydroxy analogue by making its methyl ether (i.e. methoxychlor) and thus restoring the high lipoid/water partition coefficient necessary for effect on the axon sheath.[200] The bromine analogues of DDT, namely $(BrC_6H_4)_2CH \cdot CCl_3$, $(ClC_6H_4)_2CH \cdot CBr_3$ and $(BrC_6H_4)_2CH \cdot CBr_3$, all cause the sudden increase in respiratory rate characteristic of DDT, when applied as dusts to *Oryzaephilus*. Other compounds which have induced characteristic DDT symptoms in the cockroach include *p*-dichlorobenzene, hydroquinone, and *p*-phenylenediamine, which carry Cl, OH, and NH_2, respectively, in the *para* position. It has been noted that

p-phenylenediamine and several other "pseudo"-DDT's have a special affinity for the cytochrome (indophenol) oxidase system.[124]

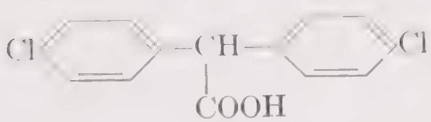


DDT DMC

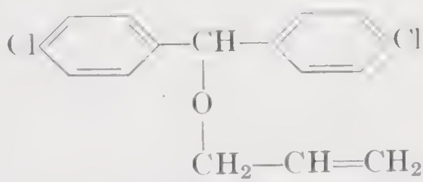
The acaricidal activity of this group of compounds must bear an entirely different relationship to molecular structure. DDT itself is not toxic to *Paratetranychus citri*, nor indeed are any analogues in which the ethane nucleus is trichlorinated. When the three chlorine atoms are removed, di(*p*-chlorophenyl)ethane is found to be acaricidal. Upon shortening of the chain, the strongly acaricidal and insecticidal di-(*p*-chlorophenyl)-methane is obtained; or upon hydroxylation the superior acaricide 1,1-bis-(*p*-chlorophenyl)ethanol appears, which has been developed commercially under the name DMC. The bis(*p*-chlorophenyl)methanol analogue of DMC is almost inactive.[113]

More remote analogues of DDT

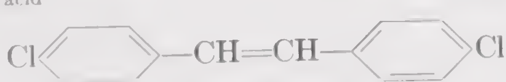
Compounds more distantly related to DDT may be synthesized by replacing the ethane nucleus with other short-chain nuclei. Oxidation of the trichloroethane nucleus of DDT to acetic acid produces a compound known as DDA, which shows weak contact toxicity and is a mediocre mosquito larvicide; the derivatives of DDA which lack *p,p'*-dichloro substitution are non-toxic. It is considered that the presence of the highly polar COOH group in these molecules destroys their contact toxicity.



p,p'-Dichlorodiphenylacetic acid



p,p'-Dichlorodiphenyl methyl allyl ether



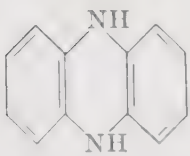
p,p'-Dichlorostilbene

The following *p,p'*-dichlorodiphenyl derivatives have shown moderate to good toxicity to mosquito or moth larvae or to adult flies: (*p,p'*-dichlorodiphenyl)-2-nitroethane, -propylene, -2.3-trichloropropylene, -methylacetylene, -1-hydroxymethylacetylene, and -methyl methyl ether.[34, 89, 126] The (*p,p'*-dichlorodiphenyl)-methyl allyl ether is not only a good anti-moth impregnant, but also an excellent residual poison for flies, although it is slow in action.[126] Triphenylmethane and its derivatives, triphenylchloromethane and tris(4-chlorophenyl) carbinol, proved to be without insecticidal action.[12, 54]

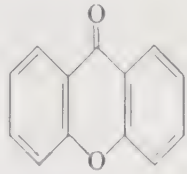
The activity of compounds in which more than one carbon atom is interposed between the two phenyl groups has also been investigated. Although benzil (ϕ-CO-CO-ϕ) is a good acaricide, it is not insecticidal, nor are its oximes or semicarbazones.[166, 180] Thus, *p,p'*-dichlorobenzil is found to show no residual toxicity to *Drosophila*. However, *p,p'*-dichlorostilbene with its ethylene linkage is a good insecticide.[126] The presence of an acetylene linkage in *p,p'*-dichlorotolane, is associated with a weak insecticidal activity, although tolane itself has proved an effective clothing impregnant for mite control. No compounds with a chain of three or more carbon atoms between the benzene rings, including several with the propylene oxide grouping, showed any more than slight toxicity.[183]

Dibenz compounds enclosing heterocyclic ring with N, O, or S

Ring with nitrogen. Dibenzpyrrole (carbazole) is non-toxic[174] and so are its derivatives, with the exception of the acaricide N-vinylcarbazole and the larvicide tetranitrocarbazole. The latter compound was used as a selective insecticide for *Clysia* and *Polychrosis* in German vineyards, under the name of *Nirosan*.[105] Acridine shows high toxicity to red spider, surpassing its analogues pyridine and quinoline,[81] and it is insecticidal to caterpillars.[54] The dihydrogenated derivative acridan is less toxic, and the 9-keto derivative acridone is almost non-toxic.[180, 18-] The diimino analogue, dihydrophenazine, proves to be one of the most toxic compounds discovered in tests on *Cochliomyia* larvae, and is the outstanding dibenz derivative.[174] Phenazine is also highly effective against these larvae.[15]



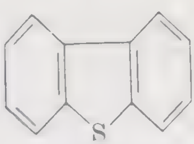
Dihydrophenazine



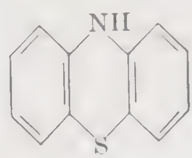
Xanthone

Ring with oxygen. Dibenzofuran is a moderately good insecticide, being almost as effective as phenothiazine against dipterous larvae. It is moderately toxic to caterpillars[63] and mosquito larvae and is acaricidal. None of its derivatives, including dinaphthofuran, show any notable activity.[13,183] Xanthene is moderately toxic, but its derivatives, including xanthydrol, are ineffective. Xanthone shows considerable toxicity to caterpillars, to the point of being a practical insecticide for codling-moth larvae. Substitution of S in the carbonyl group of xanthone to produce xanthione was found to eliminate the toxicity. On the other hand, similar substitution in the keto group of coumarin produced the highly insecticidal thiocoumarin.

Ring with sulphur. Dibenzothiophene is as toxic as phenothiazine to *Cochliomyia*,[15] shows moderately high toxicity to caterpillars[183] and mosquito larvae,[16] and is acaricidal. Its analogue thioxanthene is non-toxic to many species. Neither thioxanthene nor thioxanthone is insecticidal, and thioxanthydrol has shown toxicity only to *Carpocapsa*.[168] Thianthrene proved to have no effect on any of the species tested.



Dibenzothiophene



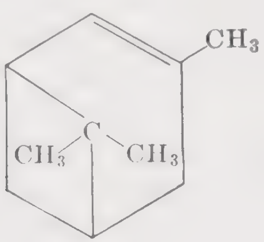
Phenothiazine

Ring with two elements. Phenoxazine is moderately insecticidal,[174] but its derivatives are ineffective.[183] Phenoxathiin (also termed phenothioxin) is highly toxic to maggots and to some caterpillars.[43,72,85,117,168,174,183] Its derivatives, including the dinaphtho analogue, are non-toxic. Phenothiazine is a highly effective larvicide for *Lucilia*, *Phormia*, *Cochliomyia*, *Culex*, and *Chaoborus* when mixed in the medium in which they live, but it shows mediocre contact toxicity to caterpillars, grasshoppers,

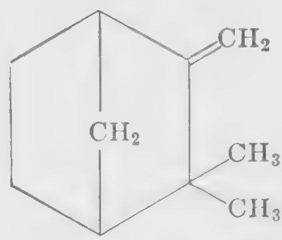
roaches, bees, or beetles. None of its derivatives are as effective, and the majority are entirely inactive.

Terpenes

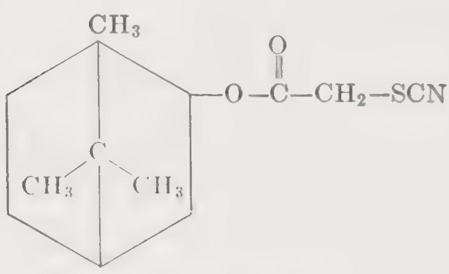
A number of highly effective insecticides have been discovered which are built on the terpene nucleus. The molecular structure of several of them is not yet clear. Crude camphor, applied by contact to the head, was an old-fashioned substitute for the killing bottle for collecting insect specimens. Whereas borneol and its acetate are non-toxic, an insecticide and acaricide has been found in the thiocyanoacetate of a mixture of secondary and tertiary terpene alcohols (mainly fenchyl and isobornyl) marketed commercially as *Thanite*.[136]



α-Pinene



Camphene



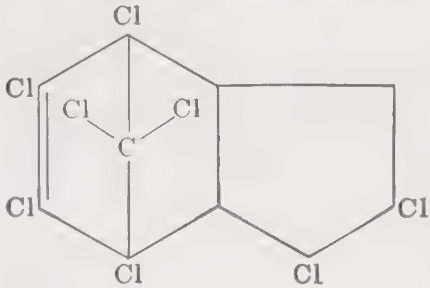
Isobornyl thiocyanoacetate

Bornyl chloride and dipentene dihydrochloride have been found to be comparable to DDT in toxicity, and 2,6-dichlorocamphane and -cymene to be synergistic to DDT; all four compounds are readily dehydrochlorinated.[35] Although bromocamphor and camphor oxime are only slightly toxic, an excellent insecticide has been found in octachlorocamphene, known as chlorinated camphene or toxaphene ($C_{10}H_{10}Cl_8$).

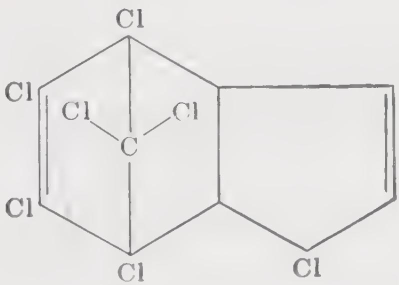
Another chlorinated terpene product containing the endomethylene group is the highly insecticidal material known as chlordane, which consists mainly of two isomers of octachloro-

4,7-methanotetrahydroindane. It too is susceptible to dehydrochlorination, whereas its non-toxic precursors lacking Cl on the cyclopentane ring are not so.[103] It is considered that this material is a mixture of closely related compounds of which a heptachlorinated terpene is the most active insecticidally. In this compound, termed heptachlor, the presence of a double bond, associated with the absence of one chlorine atom, on the five-membered ring makes it a derivative of indene rather than indane.

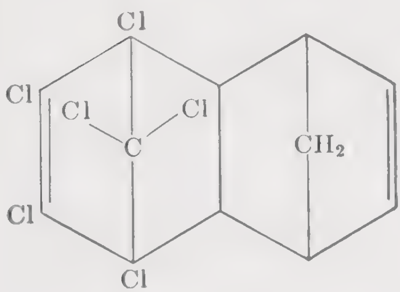
Chlordane
1,2,4,5,6,7,8,8-octachloro-4,7-methano-3a,4,7,7a-tetrahydroindane



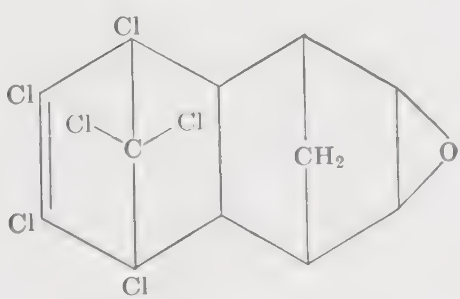
Heptachlor
1,4,5,6,7,8,8-heptachloro-4,7-methano-3a,4,7,7a-tetrahydroindene



Aldrin
1,2,3,4,10,10-hexachloro-1:4,5:8-diendomethano-1,4,4a,5,8,8a-hexahydronaphthalene



Dieldrin
1,2,3,4,10,10-hexachloro-6,7-epoxy-1,4,4a,5,6,7,8,8a-octahydro-1:4,5:8-dimethanonaphthalene



Chlordane, which may be considered a hexahydroindene as well as a tetrahydroindane, can exist as either the endo or the exo isomer, depending on the side of the six-membered ring from which the methano group projects; in fact only one isomer of the pair is present, but its identity has not yet been determined.[100] In addition it shows *cis-trans* isomerism at the 2,3 position, the *trans*(β-chlordane) being 10 times as toxic as the *cis*(α-chlordane) isomer. Whereas heptachlor is 4–5 times as toxic as technical chlordane, its hexachloro analogue is only 0.15 times as toxic as this standard.[101]

A compound with a similar configuration in the six-membered ring has been developed as the insecticide aldrin, which is a hexachlorodimethanohexahydronaphthalene; its oxygenated derivative is known as dieldrin. Heptachlor, aldrin, and dieldrin show the same extraordinarily high toxicity to insects (e.g. *Musca*, *Melanoplus*) as lindane does, and there is reason to consider that all four compounds present certain of their chlorine atoms in a similar spatial configuration.

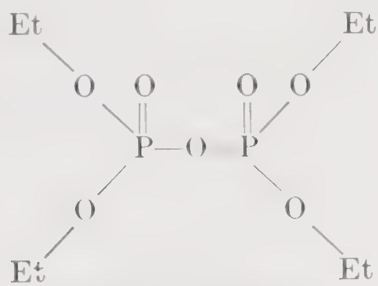
The methyl ethers of terpineol and of pinene show contact toxicity to *Musca*. The ethylene glycol ether of pinene is the most toxic of their analogues; since it shows synergistic action with pyrethrum it is known as D.H.S. Activator.[136] Other terpene-base compounds such as *Thanite*, terpin diacetate, and pine oil are also synergistic with pyrethrins.

Organic phosphates

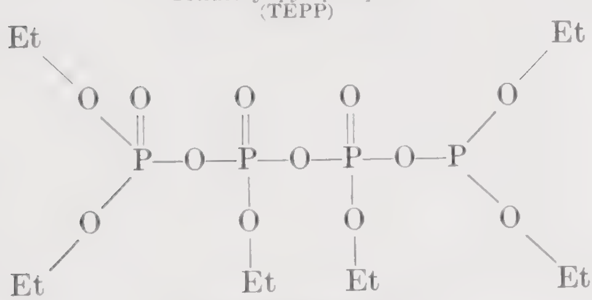
Of the alkyl phosphates, the acid phosphates, triphosphates, and phosphonates show light to moderate contact toxicity, while the di- and trialkyl phosphites are non-toxic.

The pyrophosphates, triphosphates, and tetraphosphates, however, are outstanding in toxicity, their contact effectiveness against aphids being superior to that of nicotine. In the pyrophosphates, the tetraethyl ester is superior to the propyl or butyl, while in the tetraphosphates the hexabutyl ester is superior to the ethyl- or propyl analogue.[98] The tetraethyl pyrophosphate (TEPP) is considerably more toxic than the hexaethyl tetraphosphate (HETP), so that TEPP is the only truly active constituent of commercial preparations of HETP.[64] There are

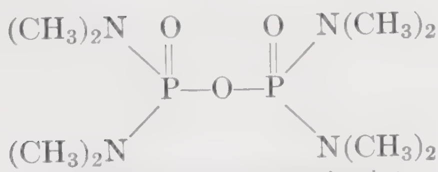
no grounds for believing that tetraethyl peroxydiphosphate (≡P—O—O—P≡) is the active constituent. The structure of hexaethyl tetraphosphate has been determined to be linear,[29] rather than the tree formula originally figured.[45]



Tetraethyl pyrophosphate
(TEPP)



Hexaethyl tetraphosphate
(HETP)



Tetrakis(dimethylamino)pyrophosphate
(OMPA)

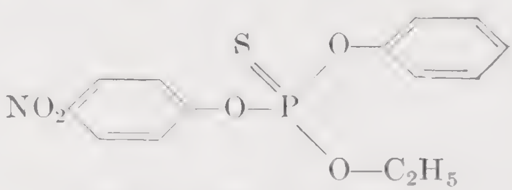
It may be noted that the less insecticidal phosphates show trialkyl or monoalkyl substitution, while the active pyro-, tri-, and tetraphosphates are dialkyl esters. The suggestion has been made that these dialkyl compounds poison the insect's glycolytic system at the point where the coenzyme adenosine triphosphate may play a part.[64]

Certain of the organic phosphates, which do not hydrolyse so rapidly in water as the compounds mentioned above, may be absorbed into plant tissues to become systemic insecticides. The progressive substitution of dimethylamino groups for the ethyl groups of TEPP results in increasing stabilization of compounds

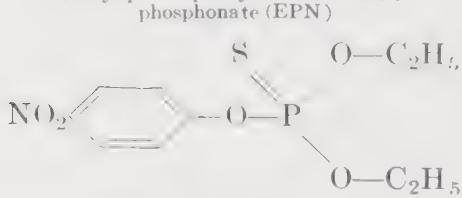
which are both systemic and insecticidal; the bis(dimethylamino) being resistant to hydrolysis by water but not by alkali, the tris being resistant to alkaline hydrolysis,[105] and the tetrakis being a stable and safe systemic insecticide developed under the name of OMPA or *Pestox III*.

On the analogy of diisopropyl fluorophosphonate (DFP), which was one of the first of the highly toxic phosphates to be discovered and studied on mammals, diethyl fluorophosphonate was synthesized and found to be a very promising insecticide.[155] By substitution of dimethylamine for the ethyl groups, the systemic insecticide bis(dimethylamino) fluorophosphine oxide is obtained, which is more powerful in this respect than OMPA but is too toxic for mammals to be used on plants.[104]

TEPP may also be stabilized by the addition of thio groups to make the corresponding thiopyrophosphate. Tetraethyl monothiopyrophosphate is stable in water, while the dithiopyrophosphate is stable in limewater.[155] Both compounds are just as insecticidal as TEPP and are less toxic to mammals.[25, 104] Tetra-*n*-propyl dithiopyrophosphate has proved more toxic than pyrethrins to *Musca*, despite being relatively non-poisonous to mice.[50a]



Ethyl *p*-nitrophenyl thionobenzene phosphonate (EPN)



Diethyl *p*-nitrophenyl thionophosphate (Parathion)

When TEPP is split into the diethyl phosphoric acids, and an aryl group substituted for the free hydrogen ion, stable insecticides are obtained. The phenyl diethyl phosphate is quite insecticidal, and the toxicity may be increased 10 times by a *p*-chloro group. It may be increased 200 times by the addition

of a nitro group in the *ortho* or *para* position, but not in the *meta*.[155] Thus the compound E-600 (para-oxon or diethyl *p*-nitrophenyl phosphate) is highly insecticidal, but it is extremely toxic to mammals. Substitution of dimethylamine for ethyl groups decreases the insecticidal power to a very low figure. Substitution of a thio group to produce diethyl *p*-nitrophenyl thiophosphate, or E-605, gives a compound that is seldom less than one-half as insecticidal,[4] is more stable, and is much less toxic to mammals, although considerably less strongly systemic.[39] To this compound, correctly termed O,O-diethyl-O-*p*-nitrophenyl thionophosphate, there has been given the name parathion; it is without doubt the most generally powerful insecticide in commercial use at present. No other dialkyl analogue is as insecticidal as parathion, with the exception of the dimethyl *p*-nitrophenyl thiophosphate.[118] From assessments of their ovicidal power for *Aphis pomi*, it is concluded that the most toxic phosphates and thionophosphates have two alkyl groups and one aryl group with a strongly electron-attracting substituent in the *para* position.[39a]

The organic phosphates show an extremely high toxicity to mites as well as to insects, which stands in sharp contrast to the low acaricidal activity of the best chlorinated hydrocarbon insecticides. Recently, 0-ethyl-0-nitrophenyl thionobenzene phosphonate (EPN) has proved to be an outstanding residual acaricide. None of the S-substituted analogues of parathion, many of which are safer to man, are more effective insecticides, with the exception of the 2-chloro analogue in the case of the squash bug.[39a]

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List of Insects Cited by Genus Only in Chapters I–V

Acronicta aceris	maple dagger moth
Aedes aegypti	yellow-fever mosquito
Agriotes spp.	wireworms
Ahasverus advena	a cucujid beetle
Anasa tristis	squash bug
Anopheles quadrimaculatus	common malaria mosquito
Anticarsia gemmatilis	velvetbean caterpillar
Anuraphis sanborni	elder aphid
Aonidiella aurantii	California red scale
Aphis rumicis	bean aphid
Apis mellifera	honeybee
Aspidiotus perniciosus	San José scale
Attagenus piceus	black carpet beetle
Automeris io	io moth
Blatta orientalis	oriental cockroach
Blattella germanica	German cockroach
Bombyx mori	silkworm
Calliphora erythrocephala	a blowfly
Carabus violaceus	a ground-beetle
Carpocapsa pomonella	codling moth
Celerio lineata	white-lined sphinx
Chaoborus astictopus	Clear Lake gnat
Cimex lectularius	bedbug
Cochliomyia americana	screwworm fly
Corethra spp.	midges
Culex quinquefasciatus	southern house mosquito
Dendrolimus pini	pine caterpillar
Dixippus morosus	stick insect
Drosophila melanogaster	vinegar fly
Dytiscus marginalis	a water beetle
Empis stercorea	a dance fly
Ephestia kuehniella	Mediterranean flour moth
Epilachna varivestris	Mexican bean beetle
Euproctis chrysorrhoea	browntail moth
Eutettix tenellus	beet leaf hopper

Euxoa segetum	European wheat cutworm
Galleria mellonella	wax moth
Glossina palpalis	a tsetse-fly
Grapholitha molesta	oriental fruit moth
Gryllotalpa spp.	mole-crickets
Heliothis armigera	corn earworm
Heliothrips haemorrhoidalis	greenhouse thrips
Hippodamia convergens	convergent lady-beetle
Hyponomeuta padella	ermine moth
Lasioderma serricorne	cigarette beetle
Leptinotarsa decenlineata	Colorado potato beetle
Limonius canus	Pacific Coast wireworm
Locusta migratoria	migratory locust
Loxostege sticticalis	beet webworm
Lucilia sericata	sheep blowfly
Lymantria monacha	nun moth
Macrosiphum pisi	pea aphid
Mantis religiosa	European mantis
Melanoplus differentialis	differential grasshopper
Melophagus ovinus	sheep tick
Myzus persicae	green peach aphid
Nematus ribesii	currant sawfly
Oecanthus niveus	snowy tree cricket
Oncopeltus fasciatus	large milkweed bug
Ornithodorus moubata	argasid tick
Oryzaephilus surinamensis	saw-toothed grain beetle
Paratetranychus citri	citrus red mite
Passalus cornutus	horned passalus beetle
Pediculus corporis	body louse
Periplaneta americana	American cockroach
Phlegethontius quinquemaculatus	northern tomato worm
Phlyctaenia rubigalis	greenhouse leaf tier
Phormia regina	black blowfly
Pieris rapae	imported cabbageworm
Plutella maculipennis	diamondback moth
Popillia japonica	Japanese beetle
Prodenia eridania	southern army worm
Pyrausta nubilalis	European corn borer
Rhagium bifasciatum	a boring beetle
Rhodnius prolixus	an assassin bug
Sarcophaga falculata	a flesh fly
Schistocerca gregaria	desert locust
Scirtothrips citri	citrus thrips
Sitophilus granarius	granary weevil
Sitophilus oryzae	rice weevil
Smerinthus ocellata	eyed hawk moth
Stilpnotia salicis	satin moth

Tenebrio molitor	yellow mealworm
Tetranychus bimaculatus	two-spotted spider mite
Thermobia domestica	firebrat, silverfish
Tinea pellionella	case-making clothes moth
Tineola bisselliella	webbing clothes moth
Tribolium confusum	confused flour beetle
Vanessa cardui	painted-lady butterfly

CHAPTER III

Susceptibility of Insects to the Entry of Poisons

General considerations

In order that they may effect a response at the appropriate site of action, it is necessary that insecticides enter the body of the victim. On the one hand the insect has a less complex organization than the mammal; but on the other it exposes a far greater surface area relative to its volume to the vicissitudes of the external environment. Thus its cuticle is of extraordinarily great importance. To serve as protection against the twin dangers of excessive water loss and drowning, the terrestrial insect is endowed with a hydrophobic cuticle which is at the same time lipophilic. Advantage has been taken of this latter quality in the application of organic liposoluble compounds as contact insecticides.

Another mode of entry for insecticides is by way of the mouth and alimentary canal. Here many insects, especially larvae, put themselves at a disadvantage by reason of their extreme vora-

ciousness. A third route of entry is afforded by their respiratory system. In comparison to the vertebrates, which have a single protected entry into the lung from orifices in the head, most insects offer many points of entry at the spiracles disposed along the length of the body. Thus the insect is susceptible not only to fumigant vapours,* but also to the inhalation of poisonous liquids of low surface tension which may be sprayed onto the body surface under open-air conditions. Thus it is generally true that any diminution of susceptibility to poisons enjoyed by insects because of their relative simplicity of organization may be countered by a less adequate degree of protection against entrance into the body.

Insecticides are generally poisonous to all multicellular animals. It has therefore been concluded that the apparent specificity of insecticides for insects is due to the fact that the insecticides have a special ability to penetrate the insect integument. When an insecticide such as rotenone, lindane, or DDT is injected into the blood or haemolymph, it has been found to show a similar level of toxicity to the mammal as to the insect (Table 1). The very great differences in contact toxicity are thus due to the fact that whereas the mammal interposes an effective barrier of protective tissue, the cuticle of the insect is an ineffective shield against these particular poisons.

TABLE 1. Toxicity of Insecticides to Vertebrates and to Insects[28]

Median lethal dose, mg/kg

	Vertebrates *		Insects †	
Compound	Contact	Injection	Contact	Injection
DDT	300–3000	12–75	5–30	5–60
Lindane	300–500	50–75	0.4–7.5	3–17
Rotenone	Very high	0.4–2	Appr. 30	6–15

* Frog, rat, rabbit, cavies, cat, and dog.
† *Periplaneta*, *Musca*, *Calliphora*, and *Aedes*.

A similar interpretation may be applied to the differences in susceptibility of various insects to contact poisons. The resistance of locusts to contact poisoning by rotenone disappears

* But no more susceptible, and often less so, than higher animals.

when this insecticide is injected into the haemolymph. The less hardened and impermeable the cuticle of the species of insects investigated, the more susceptible they will be found to be to contact poisoning by rotenone. The variation in permeability of the cuticles of a stock of *Phormia* larvae is as great as the variation in susceptibility to contact poisons normally found in insecticide testing. Again the penetrability of a chemical may be of more importance than its intrinsic toxicity in deciding whether it is a contact insecticide. In a comparison of the insecticidal action of thiocyanates, for instance, it was found that a highly poisonous but only moderately penetrating compound was less effective in killing *Aphis* than an analogue only half as toxic but showing a quarter more penetrating power.[64] In the testing of nicotinium derivatives, discrepancies in the relation of structure to toxicity could be attributed to cuticle impermeability masking the intrinsic toxicity of a compound.[147]

With insecticides the paradox may occasionally be shown of the contact toxicity exceeding the toxicity by injection. It was observed that the lethal dose of nicotine necessary for *Celerio* larvae was higher for injections than for sprays.[54] One of the nicotinium derivatives showed an even greater differential in favour of contact toxicity.[147] Certain nerve poisons may reach a site of action without entering the haemolymph at all, exerting an effect at the cuticular level on the sensory nerve endings at the hair sensilla, campaniform sensilla, the pulvilli, or the tarsal sense organs. These characteristics enhance the contact toxicity of DDT, and the figures in Table 1 suggest that lindane also shares these qualities. Conversely the injection of certain nerve drugs, e.g. acetylcholine, into the haemolymph does not result in their reaching the site of action, because of the interposition of the medullary sheath protecting the underlying nerves.

It is nevertheless generally true that poisons applied by injection not only are more toxic, but also are much faster-acting than contact applications. The onset of paralysis occurs very quickly and affects all parts of the body simultaneously. Tracheal penetration also results in faster action than cuticular penetration of contact insecticides. Stomach poisoning, however, may proceed at a slower rate than contact poisoning.[13] The toxicity of

sodium arsenate to silkworm larvae when administered by mouth is only one-quarter of its toxicity by injection, although the relationship between dosage and survival time shows a parallel course (Fig. 1).

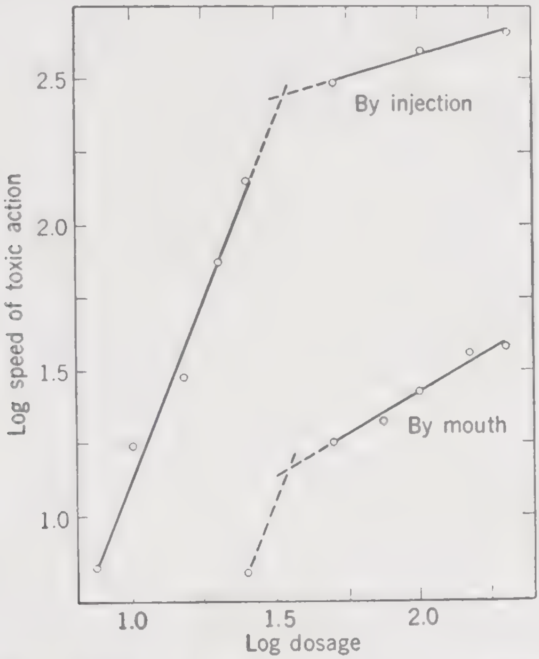


FIG. 1. Comparative speed of toxic action of sodium arsenate on *Bombyx* larvae, by injection as compared with the oral route. (From Campbell, 1925)

Classification by mode of entry

Insecticides have been classified, according to the manner in which they are administered to insects and their mode of entry into the body, into the following four groups:

Stomach: application to the food and entry through the mid-gut, e.g. arsenicals and fluorine compounds.

Contact: application to the body surface and entry through the cuticle and tracheae, e.g. pyrethrins, rotenone, nicotine.

Fumigant: application as a vapour and entry through the tracheae, e.g. HCN, chloropicrin, methyl bromide.

Residual: application to surfaces and subsequent uptake through the cuticle, especially of the tarsi, e.g. DDT, chlordane.

This is not a true classification, since any given insecticide will be found to partake of a measure of several of the types of toxicity. Nicotine, which is considered primarily as a contact insecticide, is also a stomach poison and a fumigant. Its fumigant action may occur not only by entry through the tracheae but also by penetration of the vapour directly through the cuticle. Arsenicals and fluorides exhibit a degree of contact toxicity, yet when applied by contact they also enter as stomach poisons because of the insect's cleaning movements. Chlordane is capable of showing all four types of toxicity, lindane and DDT three out of the four. These insecticides will be found to arrange themselves in different orders of toxicity, depending on which category is considered.[136]

Stomach:	Lindane > DDT > chlordane
Contact:	DDT > lindane > chlordane
Fumigant:	Chlordane > lindane > DDT

The position of an insecticide in this classification is decided by its physical characteristics. Stomach insecticides are those which have not sufficient liposolubility to be applied by contact or are not volatile enough to act as fumigants. Contact insecticides are solid or liquid at working temperatures, but they also show fumigant toxicity if their vapour pressure is appreciable, e.g. nicotine or lindane. If the vapour pressure is negligible they exhibit residual toxicity, e.g. DDT. Chlordane and parathion have vapour pressures of such a level that both types of toxicity are apparent. Pyrethrins are not volatile enough to exert an appreciable fumigant toxicity and are not stable enough to offer any residual toxicity. Contact insecticides always show stomach toxicity if the opportunity arises, except in cases where they are destroyed in digestion (e.g. pyrethrins) or fail to be absorbed (e.g. rotenone, phenothiazine).

The cuticle

The insect is enveloped by a layer of secreted material known as the cuticle, which characteristically serves as a protection against water loss. It enters the alimentary canal at both ends, corresponding to the embryonic stomodaeum and proctodaeum, leaving only a section of mid-intestine which is not plated with

cuticular material. However, even this section is protected from the food and other material entering from outside either by a continuous cylindrical membrane, the peritrophic membrane, or by a general secretion of thin sheets of similar material. The respiratory passages also are lined with cuticular material for a certain distance inwards from the spiracles.

The cuticle as it is secreted by the hypodermal cells, under the protection of the existing integument laid down in the previous instar, is clear, soft, and moist. Such a cuticle would be useless as a protective plating were it not also impregnated with fatty materials, which migrate to the outer boundary during the process of secretion or are spread over the cuticular surface by the dermal glands.[29] The thin surface layer which contains the lipoid is known as the epicuticle.

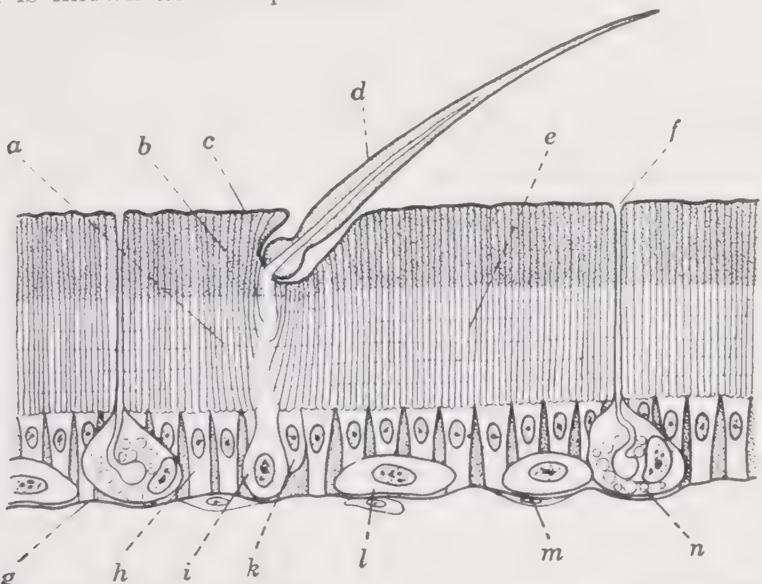


FIG. 2. Diagrammatic representation of the insect cuticle. (From Wigglesworth, 1948; for legend see this author.)

Thus when the old skin is cast the insect in its new instar emerges with a lipophilic waterproof envelope, although the cuticle as a whole is soft and pliable. In many insects, notably aquatic forms and larvae, it remains in this condition. But in others, particularly those which are active and require rigid supports for muscles and a further protection from the aerial conditions into which they embark, the cuticle quickly becomes hard

and dark on removal of the old skin. The resultant condition is that of sclerotization, and results from a process of tanning of the protein by quinones. The tanned layer, which is generally confined to the outer portion of the cuticle, forms a second protective barrier between the insect and its environment. It is known as the exocuticle, and the remainder of the cuticle, which has not been sclerotized, is termed the endocuticle.

A diagrammatic representation of the three main cuticular layers is given in Fig. 2, and their relative thickness in eight species of insects is shown in Table 2. For detailed accounts of the cuticle of insects and the integument of arthropods the reader is referred to monographs by Wigglesworth [164] and Richards.[108]

TABLE 2. THICKNESS OF CUTICULAR LAYERS, MICRONS

Species	Endo-cuticle	Exo-cuticle	Epi-cuticle	Total
Periplaneta americana (A *) [109]	28	10	2	40
Culex pipiens (L *) [109]	2	..	0.05	2
Sarcophaga falculata (L) [23]	100	..	4	104
Acronicta aceris (L) [70]	52	4	0.8	57
Rhagium bifasciatum (L) [70]	31	6	0.5	38
Carabus violaceus (L) [70]	9	8	0.3	17
Empis stercorea (A) [70]	8	3	0.8	12
Dytiscus marginalis (L) [70]	25	3	0.6	29

* (A) adult; (L) larva.

The epicuticle. This surface layer comprises between 1 and 7% of the total cuticular thickness. It is characterized by a resistance to strong acids, which dissolve the remainder of the cuticle. On the other hand, it is dissolved by strong alkalis, and its structure is impaired by fat solvents such as chloroform and acetone. It shows a similarity to the cuticle of the plant in many properties, even to staining with Sudan III and Black Sudan.[69]

Typically the epicuticle consists of a thin layer of tanned protein impregnated on its outer surface by lipoid or wax. An artificial substitute may be readily made on a framework of voile by cooking a gelatin solution with benzoquinone to form tanned protein, and then applying beeswax from chloroform solution to give the lipoid layer.[6] In *Periplaneta* two layers of epicuticle

may be distinguished, a very thin (0.3 μ) outer layer containing lipoid and a thicker (1.7 μ) inner layer which lacks it.[109] Since no trace of lipoid can be found in the remainder of the cuticle of the roach, it is considered that the epicuticular lipoid is derived from the external secretion of dermal glands, the wax spreading across the outer surface.[104]

The alternative suggestion has been made that the lipoid may have been carried out to the epicuticle by the pore canals. Or it may have been secreted in the general moist matrix of the cuticle and then attracted to the surface, particularly if it is sclerotized. Consideration of the permeability of cuticle has led to the postulation that lipoid tracts extend inwards from the epicuticle,[61] but present evidence indicates that the cuticular lipoid is confined to the epicuticle.[5]

It is considered that the loss of hydrophilic properties associated with the tanning of the epicuticular protein renders it more susceptible to impregnation by lipoids, with which it combines in a lipoprotein association, to be oxidized and polymerized *in situ*.[104] The resulting product, which contains fatty acids, aliphatic alcohols, and possibly also cholesterol, has been termed cuticulin.[157] From studies of the waxes of coccids and the epicuticular material of silkworm larvae, it is considered that the cuticular lipoid is a mixture of paraffins, fatty acids, and alcohols whose average chain length is C_{30}, ranging from C_{24} up to C_{36} and occasionally as far as C_{70}.[5]

The epicuticle is typically smooth, but it may show minute spines or processes.[70] It may be overlaid with grease (blattids) or with a heavy layer of wax (*Dytiscus*, coccids, and psyllids). It may also be overlaid with a granular *Sekretschicht* (Coleoptera) or a very thin cement (*Rhodnius*) derived probably from the dermal glands.[158]

The lipoid layer of the epicuticle may range in thickness down to 0.01 μ in *Nematus* larvae, which is still sufficient to contain 30 monolayers of wax arranged vertically. An extreme thickness of over 1 μ is found to overlay the puparium of *Calliphora*. The hardness of the wax is a function of its melting point, which may vary from 40° C in the soft wax of *Nematus* larvae to 60° C in the hard wax of *Rhodnius*; some lipids may be fluid

greases at room temperature, as in *Blatta*. There is evidence that the lipoid is closely packed on the surface, with the hydrocarbon side-chains projecting outwards like the pile of a carpet, and the reactive carboxyl and hydroxy groups attached to the underlying protein.[5]

The normal function of the epicuticular lipoid is to prevent the passage of water outwards through the cuticle, thus protecting the insect against desiccation. Conversely, since any water that contacts the epicuticle gathers itself into droplets and rolls off the insect, it prevents moisture or rain from soaking the respiratory apertures. It is of interest that the larva of the petroleum fly (*Psilopa*) has a hydrophilic and thus lipophobic epicuticle, probably because it is not impregnated with lipoid.[140] It should also be pointed out that some coccid and adelgid waxes are hydrophilic as a consequence of their free keto groups.[58] The epicuticle of the larva of *Culex pipiens* is also hydrophilic, being stainable by haemotoxylin.[109] The epicuticular impregnants in the larvae of *Calliphora* and *Phormia* are also hydrophilic. If a *Calliphora* larva is secured close against a larva of *Tenebrio*, the former has the power of drawing water out of the latter insect.[60]

The endocuticle and exocuticle. When the endocuticle is freshly laid down it is colourless and pliable;[159] consisting of 70% water, it contains crystallites of chitin, arranged parallel to the cuticle surface but freely rotatable in that plane, embedded in a matrix of soluble protein[36] (arthropodin[164]). After they have been secreted, the chitin and protein of the endocuticle separate into horizontal layers, or lamellae. In the endocuticle of *Periplaneta*, dense layers of chitin-protein conjugate, 0.15 μ thick, alternate with more transparent layers of chitin alone, 0.3 μ in thickness.[109] These lamellae are strongly developed in the cuticles of species like *Gryllotalpa* and on the pronotal excrescences of *Stethophyma*. In addition, vertical striping is detectable in the cuticle of femora and mandibles of *Gryllotalpa*.[18]

The tanning process whereby the outer portion of the endocuticle is transformed into the hard exocuticle or *Pigmentschicht* has been fully studied in the fly and the roach. The aromatic quinones responsible for the process have been ultimately derived from the amino acids tyrosine and phenylalanine of the

haemolymph. These are first oxidized to dihydroxyphenylalanine (DOPA)* by the tyrosinase of the oenocytoids, which is deaminated in the hypodermal cells to produce dihydroxyphenyllactic acid and the dihydroxyphenylacetic and benzoic acids. These are converted by the phenoloxidases of the outer cuticle to their corresponding dioxyphenyl compounds or quinones, which condense with the free amino groups of the proteins.[101] The loss of free hydrophilic groups renders the protein insoluble, forces out water from the more closely packed materials, and anchors the micelles of chitin so that they can no longer rotate.[36] A concomitant process is the production of the brown and black melanin pigments. Thus the exocuticle so produced is dark and hard, dry and rigid.

The exocuticular sclerotization may involve as much as one-quarter of the thickness of the endocuticle of *Gryllotalpa* and *Periplaneta*, and even more in certain Coleoptera. This process may take place in the form of a continuous sheet over entire sclerites, leaving only the intersegmental folds unsclerotized.[18] In some species, cuticular sclerotization may be restricted to a close array of minute round dots, or a regular mosaic of hexagonal microsclerites as in *Tenebrio*. In certain beetles the intersegmental folds are also sclerotized to produce a series of cones whose apices point inwards, imparting a rigid protection on the outside and yet allowing flexible movement on the inside.[69]

Pore canals, dermal glands, and sensilla. The cuticle of most insects is minutely perforated with a number of little canals or processes reaching from the hypodermal cells almost to the cuticular surface. They are overlaid by the lipoid layer of the epicuticle, through which they may be seen as a stippling of minute punctations. In *Periplaneta* these pore canals extend to the boundary of the epicuticle,[109] but in *Rhodnius* and *Melophagus* they penetrate as far as the outer layer of the epicuticle.[5] The canals are not straight but spiralled or helicoid (Fig. 3), and in some species (*Bombyx*, *Sarcophaga*) they branch distally to give a tufted appearance.[22]

* The abbreviation DOPA correctly applies to 3,4-dioxyphenylalanine, as originally termed by Bloch [*Z. physiol. Chem.*, **98**:226 (1917)].

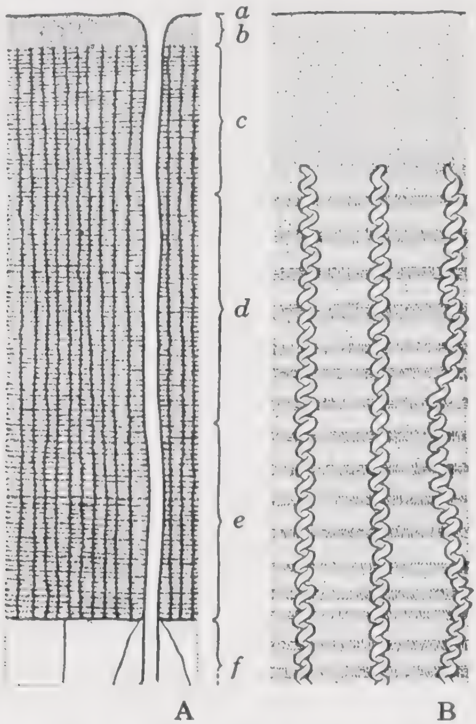


Fig. 3. Pore canals and dermal gland duct. A. Section of cuticle of *Periplaneta:* *a* and *b*, outer and inner epicuticle; *c*, exocuticle; *d* and *e*, outer and inner endocuticle; *f*, position of hypodermis. Laminae stippled; pore canals spiral lines. ×1700. B. Diagram of outer 9 μ of cuticle, showing helical pore canals. ×8500. (From Richards and Anderson)

When freshly formed by the cytoplasmic processes of the hypodermal cells, the pore canals contain fluid which stains with eosin.[22] In *Rhodnius* this fluid is considered to be protoplasm,[159] in *Periplaneta* a clear aqueous secretion.[109] As the cuticle ages, this fluid is withdrawn and may be replaced by chitinous material from the surrounding cuticle which solidifies into little rods.[22]

In the cuticle of *Sarcophaga* larvae the density of pore canals has been determined to be 15 thousand per sq mm, equivalent to about 50 canals to each hypodermal cell.[22] In *Periplaneta*, there are about 300 per hypodermal cell; their diameter being 0.1–0.2 μ, they comprise about 5% of the volume of the cuticle.[109] Pore canals occur very sparsely in the cuticle of *Carpocapsa*

larvae,[66] and they are completely absent from the cuticle of mosquito larvae.[109]

The cuticles of many insects are perforated by the ducts of dermal glands which secrete wax or grease (Blattidae), granular incrustations (Coleoptera), or odorous materials (Lepidoptera). These ducts offer a relatively broad channel to the exterior. They are, however, never particularly abundant on the cuticular surface.

In many insects, especially sclerotized active forms such as flies, bees, and wasps, the cuticle is beset with hair sensilla. These are inserted in little circular membranes, the areolae, which are extremely thin in order to allow free movement of the sensilla. In unsclerotized caterpillars the setal membranes are inserted in more rigid plaques. Other sensilla consist of walnut-shaped domes projecting slightly from the cuticle, and are known as campaniform sensilla. They have been studied on the legs of roaches, where they are particularly abundant on the trochanters, which have 75, as compared with 8 on the femur, 11 on the tibia, and 7 on the tarsus.[122]

Permeability of the cuticle

That the penetration of insecticides can occur directly through the cuticle, independent of entry *via* the tracheae or the alimentary canal, has been demonstrated by applying wax or glass cells to limited areas of cuticle, by exposing only the appendages, or by plugging the spiracles and excluding the mouth and anus by collars. The penetration of nicotine vapour through the abdominal cuticle of *Heliothis*,[117] and of the derris toxins through the body wall of *Bombyx*, has been demonstrated in each case when the spiracles have been sealed to preclude tracheal entry.[141] It has been pointed out that the most effective contact poisons are soluble in lipid solvents. However, even oil-insoluble materials such as arsenicals and fluorides are capable of entering through the cuticle. It is considered that this is due to a constant slow secretion of moisture on the cuticle surface which may be slowly reabsorbed. The relative value of the cuticular surface and the tracheae as points of entry has not yet been established for any species.

The cuticle may be looked upon as a series of barriers. The outermost barriers are provided by **hairs,** which have been found to impart a relative immunity to contact dusts. Hairy caterpillars were found to resist contact poisoning by rotenone or veratrin dusts, requiring an insecticide of high mordant power such as DNOC.[93] The heavy sclerotized elytra of beetles, with their columnae enclosing air spaces, may be taken to constitute a protective umbrella for the abdominal cuticle beneath.[70] The wings of other insects generally give no protection and may be themselves points of entry.

Another peripheral barrier is provided by cuticular **wax,** secreted as woolly threads in aphids and coccids, and united to form a single plate in the armoured scales.* This armour in *Aspidiotus* is sufficient to prevent the penetration of aqueous lime-sulphur. Waxy layers are found on the abdomen in fulgorids, cicadids, and *Apis*, and on aquatic Hemiptera and Coleoptera. Dense wax cover the pupae of many Lepidoptera. In some groups (reduviids, tenebrionids) the wax serves to incorporate grains of sand.[70] It is evident that these protective devices cannot be overcome by aqueous sprays but necessitate the application of oils of high solubility and low volatility and viscosity.

The outer barrier of the cuticle proper is the **epicuticle,** whose importance is considerably greater than its meagre thickness would indicate. Its function is to exclude water and hydrophilic substances while admitting lipophilic substances, and it confers on the cuticle the ability to keep out highly dissociating compounds while admitting those with little or no dissociation. If the lipoid of the epicuticle is removed by saponification in alkali, this selective action is destroyed and all substances are found to penetrate at an equally rapid rate, and the specific differences between cuticles of different insects disappear.[3] A similar saponification effect is evidently caused by cuticular application of lime, which increases the contact efficacy of sodium fluoride powders.[53] Dissolution of the lipoid epicuticle by treatment of the surface of the insect with chloroform [5,86] or ether [159] increases the permeability of the cuticle to pyrethrins and other contact

* In certain Diaspinae, the exuviae are incorporated into the armour, whereas certain Coccinae have a heavy exocuticle.

poisons. Immersion of the isolated cuticle in boiling water increases its permeability but does not destroy its selective action.[58]

The next barrier is provided by the **exocuticle**, the tanned and hardened outer portion of the endocuticle. It is generally observed that heavily sclerotized insects such as adult beetles show more resistance to contact insecticides than unsclerotized aphids or caterpillars. The highly resistant stick insect has a dense hard exocuticle and a general cuticular structure similar to that of beetles.[66] Cuticular penetration in these types of insects takes place mainly at the intersegmental membranes;[71,90] only immediately after a moult is the cuticle vulnerable as a whole.

The **endocuticle** itself interposes a thick barrier to protect the underlying hypodermal cells, although it is considered by some workers that once a contact poison reaches the moist endocuticle the battle for entry is won.[153] However, the thicker the endocuticle of *Rhodnius* nymphs, the longer is the time required for pyrethrins to take effect.[159] The steep increase in resistance of caterpillars as they mature to the last larval stage may be correlated with a considerable increase in cuticle thickness.[96]

Once the cuticle is penetrated, the contact poison may exert a direct effect on the hypodermal cells, as has been shown for DNOC[133] and pyrethrins[67] in certain insects. It may destroy the haemocytes in the body cavity, as in contact dusts of arsenite.[71] Or it may be carried by the haemolymph to be deposited in all the tissues. The radioactive bromine analogue of DDT, applied to the metathoracic tergite of three species of insects, was found to have penetrated to all tissues, including the brain.[11] Pyrethrins, which, like DDT, are extremely water-insoluble, were nevertheless sufficiently soluble in cockroach blood to make it toxic when applied to other roaches of the same species.[121]

However, transport of pyrethrins through the body of the insect is considered mainly to occur along the nerves, particularly along the lipoid sheaths, with which they show a high degree of affinity.[61,63,66] When applied to the cuticle they preferentially enter the trichogen cells at the bases of the hair sensilla,[150] which are in direct communication with sensory nerve endings. The same mode of entry has been considered to apply

to DDT, in view of the great sensitivity of the pulvilli and tarsal chemoreceptors on the leg extremities.[50, 125]

Vulnerable points of entry through cuticle

Generally the most vulnerable regions for the contact application of insecticides are the head and thorax, since here the insecticides can most quickly reach the vital centres. When nicotine or kerosene is applied to *Tenebrio* larvae, the most rapid response is obtained by contact to the antennae and the mesothoracic ventrum; with coconut fatty acids, to the mouth-parts (Table 3). With all three poisons, the slowest response is given by contact to the anal region. When the cockroaches *Blattella*, *Blatta*, and *Periplaneta* were treated with these compounds, the most rapid reaction was obtained on application to the ventral cervical region.[90]

TABLE 3. Point of Application of Contact Poisons and Rate of Response of *Tenebrio* Larvae [90]

Average time elapsed to onset of convulsions, min

Position	Application	Nicotine	Fatty Acids	Kerosene
Head	Antennae	2.6	14.4	Neg.
	Mouth-parts	13.0	3.2	48.8
	Ventrum head-thorax	3.6	.	....
Thorax	Ventrum Pro.-Meso.	1.2	15.8	19.4
	Ventrum-Meso.-Meta.	4.8	10.6	8.4
	Ventrum Meta.-Abd.	24.4	11.8	22.6
Abdomen	Ventrum I-II	10.0	16.4	....
	Ventrum II-III	....	....	39.6
	Anus	50.2	37.6	49.4

Caterpillars treated with pyrethrins react much more rapidly when contact is made to the head than to the posterior part of the body. The elapsed times intervening between contact and response (in this case, regurgitation) for *Phlegethontius* larvae were as follows: last abdominal dorsum, 25 min; head, 8 min; injection into haemolymph, 2 min.[17] Similar experiments with pyrethrins on *Smerinthus* larvae revealed the following times to the first noticeable response: two last segments, 50–70 sec; first

two segments, 25–30 sec; application to the dorsum was faster to elicit a response than application to the pleura.[66] When nicotine sulphate was injected into *Celerio* larvae, the elapsed time to paralysis was in direct proportion to the distance from the head of the point of injection.[54]

The cuticular grease of cockroaches may serve to spread pyrethrins, insecticides which it can dissolve.[61] Borax and fluoride dusts have been found to accumulate in the ventral region between the coxae of the legs.[127] It is on the ventrum that the contact insecticide comes closest to the nerve cord, being separated from it only by the epidermis and basement membrane.[65]

The mouth-parts, individually and collectively, have been shown to be routes of entry for pyrethrins in those insects which have been studied.[66] A dose of 0.1 μg, which resulted in only 40% knockdown of *Musca* when applied to the thoracic tergite, caused 100% knockdown when applied to the mouth-parts.[167] It is suggested that paralysis of the mouth-parts may be the most significant action of rotenone sprayed on the food of *Bombyx*.[37] The antennae were found to be one of the fastest routes of entry for sodium arsenite dusts on locusts,[71] as they were for nicotine and kerosene in the case of *Tenebrio*.[90] They are also a route of entry for pyrethrins; it is curious that the grasshopper *Tachycines*, so treated, may occasionally bite off the antenna and survive.[66] Nicotine applied to the tips of the antennae of cockroaches proved ineffective but became toxic when application was made within the first 20 proximal segments.[90] This insecticide was effective when it was applied to the antennal clubs of butterflies, but the onset of paralysis was slower than if contact was made at the bases.[99]

The wings may also serve as a route of entry. Application of pyrethrins to the wing tips of bees, wasps, or butterflies engenders the usual sequence of excitation, paralysis, and death.[66] The wings of butterflies also serve as a mode of entry for nicotine, since their veins contain circulating haemolymph. Wings of other orders of insects which lack haemolymph circulation, such as certain Orthoptera, do not allow toxic symptoms to materialize.[12] The insecticide DNOC is entirely without toxic effect when applied to the wings of *Locusta*,[65] although it has been

demonstrated to migrate laterally along the cuticle of butterfly wings.[133] The hardened anterior wings of *Periplaneta*, however, which have haemolymph circulation, can absorb the vapours of nicotine, pyridine, or piperidine in lethal quantities.[117]

The legs are the most vulnerable region for contact poisoning of *Locusta* by DNOC; there it is twice as effective as on the head or abdomen.[65] The posterior legs of *Melanoplus* can take up a toxic dose of nicotine from vapour treatment,[117] and the legs of *Macrodactylus* can serve as a route of entry of pyrethrins from aqueous suspensions.[47] The trochanters on the legs, which bear the campaniform sensilla, have been deduced to be the most vulnerable regions of the cockroach to DDT poisoning, but pyrethrins applied to this region are without effect.[124]

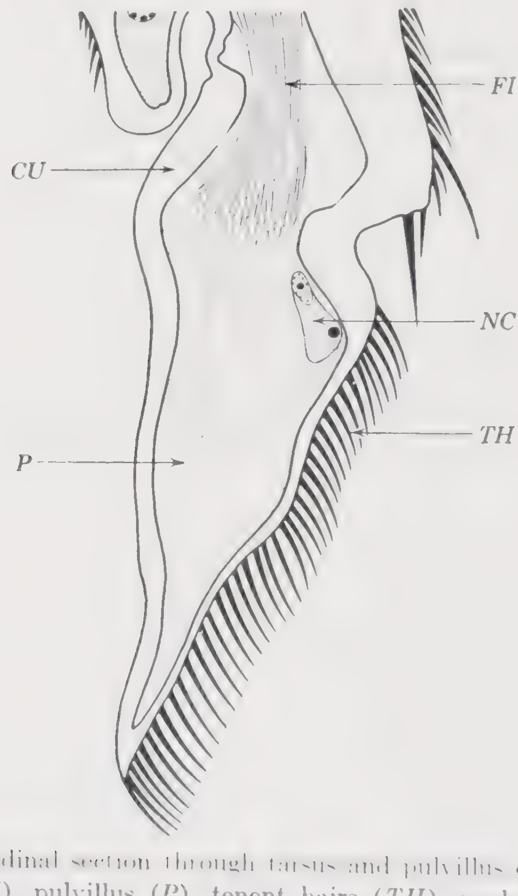


FIG. 1 Longitudinal section through tarsus and pulvillus of *M. sex.*, showing cuticle (*CU*), pulvillus (*P*), tenent hairs (*TH*), nucleus of giant cell (*NC*), and bundle of nerve fibres (*FI*). (From Sarkaria and Patton)

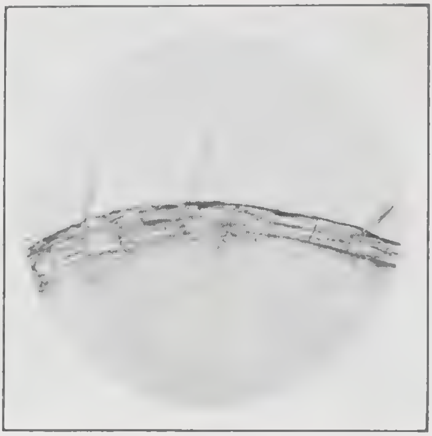
The tarsi, on which the insect walks, form a very vulnerable point in flies, mosquitoes, and the honeybee for entrance of DDT.* Here only a thin cuticle covers the cells of the tarsal chemoreceptors.[50] Moreover, the pulvilli on which the housefly walks contain a gland cell, opening to the outside by hollow tenent hairs, which produces a secretion capable of dissolving DDT, and connecting with a nerve bundle passing up the leg (Fig. 4).[125] Contact of the pulvilli of *Glossina* with pyrethrum causes almost instantaneous paralysis; with DDT, contact for 2 sec is enough to ensure death at some time later.[101] Methylnaphthalenes are more toxic to *Epilachna* and *Macrosiphum* when applied to the surface on which the insect walks rather than directly to its body.[135] Rotenone and DDT penetrate the feet of the tick *Ixodes* more readily than the dorsum.[10] But with the insecticide chlordane, whose active constituents are probably not neurotoxic, the pulvilli are no more vulnerable as a point of entry than any other part of the cuticle of *Musca*. It has been found that subsequent to application of DDT powdered crystals to the feet, the fly will spread the material all over its body, and into its mouth and digestive tract, by cleaning movements.[51] A similar migration of powdered poisons was observed on the surface of the cockroach.[127]

Whereas permeability is a function of the entire cuticular area in larvae of Lepidoptera, Diptera, and certain Coleoptera, it is restricted to the unsclerotized intersegmental membranes in adult Coleoptera and pupae of Lepidoptera, Coleoptera, and Hymenoptera, as evidenced by studies on the cuticular diffusion of carbon dioxide.[139] When sodium arsenite dusts were applied to the cuticle of *Schistocerca*, the points where entry was the most rapid proved to be the intersegmental membranes.[71] Nicotine affected *Tenebrio* larvae the quickest at the ventral intersegmental membrane between the pro- and mesothorax.[30]

The cuticle has been found to be considerably more permeable in the spots which bear the hair sensilla.[91] Penetration of dyed solutions through the cuticle of *Tenebrio* occurred mainly at the

*In the housefly, the labellum proved to be a more important point of entry than the tarsi (R. W. Fisher, 1951; Ph.D. Thesis, Macdonald College, McGill University).

trichogen cells[166] (Fig. 5). Pyrethrin solutions appeared to enter through the setal membranes or areolae surrounding the bases of the hair sensilla.[66] DDT induced symptoms of poisoning in *Musca* when it is applied to the proboscis, antennae, genae, halteres, and wing veins, which bear sensilla, but it failed to do so when applied to the thoracic tergites, abdominal tergites, abdominal sternites, and wing cells, which do not bear sensilla; here it is considered that this insecticide penetrates the unsclerotized areolae and intersegmental membranes.[155] When oils were applied to the cuticle of *Rhodnius* nymphs, subsequent staining with Black Sudan B showed that they penetrated chiefly around the bristles and plaques. Oil applied to *Rhodnius* adults, however, penetrated only by way of the ducts of the dermal glands (Fig. 6). In newly moulted nymphs or adults, penetration occurred generally over the cuticular surface.[159]



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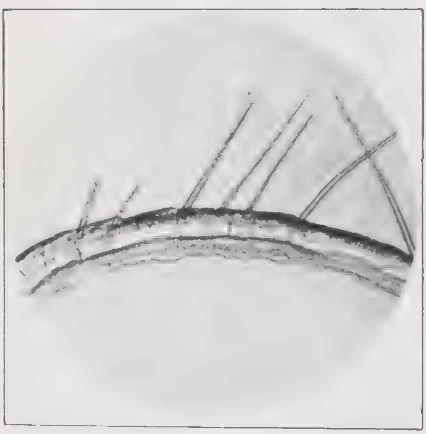


B

FIG. 5. Cross section of cuticle of *Tenebrio* larva. A. Untreated. B. Treated with pyrethrum extract dyed with Sudan III; note the staining of hypodermal and trichogen cells. ×200. (From Wilcoxon and Hartzell, 1933)

The pore canals, which may be regarded as perforations of the cuticle, are considered to aid cuticular penetration. The entry of oils has been visually detected in the pore canals of roach cuticle which has been scraped clean of hypodermis,[91] although this result may have been an artifact due to the emptying of the canals of their normal contents during preparation of the material. Entry of highly viscous oils into the pore canals

of fresh roach cuticle could not be detected under the electron microscope.[109]

If the pore canals of *Rhodnius*, which are normally tortuous, are straightened, shortened, and widened by stretching the cuticle (which can be done by plugging the anus of the insect), the rate of penetration of pyrethrins shows a threefold increase.[159] It is concluded that though the canals could hasten the process, penetration of oil takes place mainly through the matrix of the cuticle, as it must do in mosquito larvae, which lack pore canals.

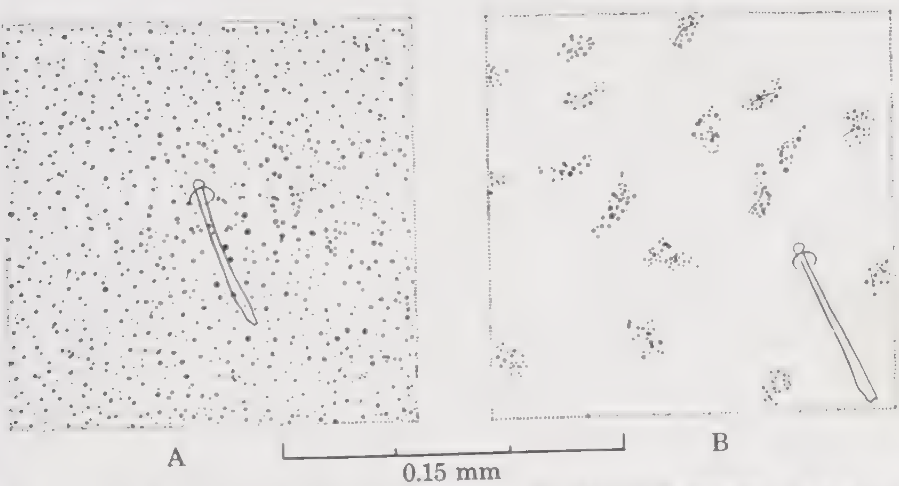


FIG. 6. Surface view of abdominal cuticle of *Rhodnius* exposed to a dyed heavy oil. A. One day after moulting, oil droplets in epidermal cells. B. Four days after moulting, oil droplets in the dermal glands only. (From Wigglesworth, 1942)

Penetration of the cuticle by insect poisons

The cuticle of insects is impermeable to strongly dissociating compounds, a property contributed by the lipoid epicuticle. Isolated larval cuticles of both aquatic and terrestrial Diptera were found to be permeable to the undissociated compounds mercuric chloride and ethyl alcohol, and to the weakly dissociated acetic acid and ammonium hydroxide, while being impermeable to the strongly dissociated hydrochloric acid and sodium hydroxide. Saponification of the epicuticle allowed all these compounds to penetrate equally rapidly.[3] On the other hand, the epicuticle has proved to be not so much a barrier as a receptor for strongly lipophilic substances. The presence of epicuticle renders the

cuticle permeable to the basic stain Congo red; if it is removed the dye can no longer penetrate.[3] The relative toxicities of a series of fatty acids to mosquito larvae (as indeed to other insects) fall in the same order as their lipoid solubilities.[59] The fat-soluble insecticides such as nicotine, pyrethrins, DDT, and hydrogen cyanide exert a more rapid contact action than the fat-insoluble arsenicals and fluorides.[58]

Whether the poison is lipophilic or not, the rate of entry of the undissociated molecule is much faster than that of the dissociated ionic component. *Culex* larvae are killed much faster by sodium arsenite in solution at pH 5, where the arsenic is in the form of undissociated arsenious acid, than at pH 11, where it is contained in dissociated arsenite ions.[56] The rate of entry of this material through the cuticle of *Calliphora* larvae is proportional to the content of the undissociated acid.[120]

The insecticide DNOC (dinitro-*o*-cresol), an acid due to its phenolic group, is highly dissociated at neutrality and completely undissociated at pH 2. When applied in 0.12% aqueous solution to *Ephestia* eggs, it proved to kill every one at pH 2, but none at all at pH 5. If the intermediate pH's are plotted against the percentage mortalities induced by them, the resulting curve will be found to follow very closely the dissociation curve of DNOC as measured photometrically (Fig. 7). The salts of DNOC, since they are alkaline or at least not acid, are much less effective than the free acid; the ammonium salt shows least reduction in toxicity since it loses alkalinity by volatilization of ammonia. The problem of pH in oil solutions or emulsions of DNOC is less pronounced, but it is still material.[26]

Nicotine as a free alkaloid is a weakly dissociating base; its water-soluble salts, such as the sulphate, are highly dissociated. Aqueous solutions of nicotine sulphate cannot kill the honeybee when applied as a spray; indeed nicotine alkaloid applied in water was found not to penetrate the cuticle of the insects studied.[81] However, if soap spreaders are added, nicotine alkaloid is found to be more effective against *Apis* than the same amount of nicotine as the sulphate.[79] Basic solutions containing nicotine alkaloid kill mosquito larvae more rapidly than acidic solutions, where it is in ionic form. A more striking circumstance is that nicotine is absorbed faster into *Periplaneta* from vapours of the

undissociated alkaloid than from immersion in more concentrated aqueous solutions of nicotine sulphate.[118] On the other hand, both molecular nicotine and ionized nicotine paralyse and kill *Periplaneta* at equal rates when they are injected into the body fluid, showing the difference to have been due to the rate of cuticle permeability.[82] The related alkaloid anabasine, when applied as a contact spray in alkaline solution, where it is a free base, has been found to cause twice as much mortality to *Aphis* as an equivalent solution of anabasine sulphate.[64]

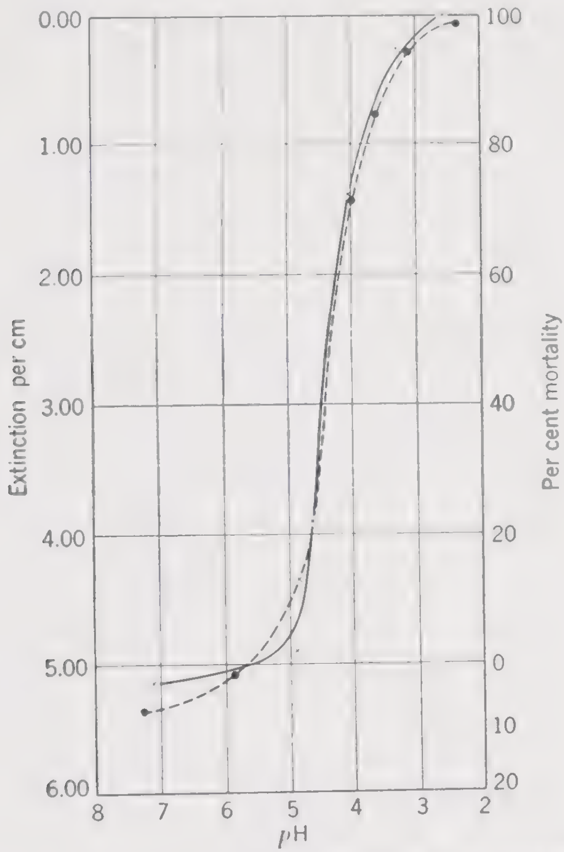


FIG. 7. Relation between contact toxicity and dissociation of DNOC. Dotted line, dissociation measured photometrically. Solid line, percentage mortality of *Ephestia* eggs. (From Dierick)

To the factor of liposolubility as aiding cuticular penetration must be added that of surface activity. That increased contact toxicity accompanies increased surface activity in ascending the

series of fatty acids and aliphatic alcohols has been demonstrated in sprays against aphids (see Chapter II). It has been reported that the contact toxicity of pyrethrins is enhanced when they are applied in water, which allows full advantage to be taken of their surface activity to collect on the cuticle-water interface.[61]

Cuticular penetration by DDT

The mode of entry of DDT through the cuticle is of particular interest because of the peculiar facility with which it occurs. This insecticide behaves as if the cuticle barrier were not there, since the lethal dosage for contact application scarcely exceeds that established for injection (see Table 1).

Moreover it has been found that DDT has a peculiar affinity for chitin. Isolated arthropod cuticle, and, even better, purified chitin have the ability to adsorb DDT out of aqueous suspension.[111] This property is not shared by cellulose or silica, and wool shows it only slightly. The fluoro, bromo, iodo, and methoxy analogues of DDT are adsorbed by chitin to an equal degree.[76] Thus its peculiar contact properties apply only to those invertebrates which have a chitinous cuticle. This principle of cuticular entry is radically different from that already discussed, namely solution in the lipoid epicuticle and partition thence directly into the underlying aqueous layer. It will be appreciated that DDT, which is liposoluble as well as chitin-adsorbable, partakes of the benefits of both principles of cuticular penetration.

It is considered that DDT is adsorbed on to the chitin micelles,[111] where its molecules are oriented,[16] and penetrates by migration along the boundaries of the intermicellar spaces. This process is analogous to the observed migration of adsorbed molecules along the surfaces of solids. The initial adsorption process would be expected to show a negative temperature coefficient.[111]

It has been observed that if larvae of *Aedes* or *Chaoborus* are exposed to very low concentrations of DDT at graded temperature between 10° and 30° C, the mortality rate is higher as the temperature is lowered. The reverse is the case when DDT

is applied in high dosages or injected directly into the haemocoele, and the temperature coefficient thus is positive. It is considered that the negative temperature coefficient obtaining on contact application of low dosages is a function of the initial concentrating action of the chitinous cuticle by adsorption of DDT. The subsequent penetration through the cuticle, and the action on the tissues, show the usual positive coefficient.[34] It is a characteristic of drug action that the temperature coefficient between 10° and 30° C, although variable, is always positive or greater than unity. *Calliphora* larvae, which are resistant to contact-applied DDT at 20° C, are susceptible to its entry at 36° C, provided that detoxification is prevented by a subsequent return of the insects to 20° C.[62]

It would be of interest to establish how far other insecticides share this property of higher contact action at lower temperatures. Lindane resembles DDT in exerting toxicity by contact as if the cuticle interposed no barrier.[28] All insecticides tested on adults of *Tribolium castaneum* (DNOC, pyrethrins, nicotine, and lauryl thiocyanate as well as DDT) were found to show greater contact toxicity at 60° than at 80° F.[100] However, since no parallel injection experiments were made, it is impossible to conclude whether the result was due to a quality of the cuticle or to the reduced rate of detoxification or excretion of the poison at the lower temperature.

Effect of the spray carrier on cuticular penetration

In order to reduce hazards to plant life to a minimum, insecticides are frequently applied in aqueous suspension as "wettable powders." However, their inferiority to oil-in-water emulsions or oil solutions in giving direct contact kills has frequently been noted. The addition of oils (especially peanut oil) to suspensions of rotenone was found to greatly enhance its toxicity to *Anasa*, *Oncopeltus*, and *Murgantia*.[38] Sprays of DDT in benzene solution were 4–6 times as toxic to *Macrosiphum* as aqueous suspensions of this insecticide.[138] The addition of paraffins or cycloparaffins (naphthenes) to indene increased its toxicity to *Cimex*.[59] Phenol dissolved in refined paraffin oil paralyses the tick *Ixodes* more rapidly than when it is applied in aqueous solution.[70] In

many cases oil solutions of chlordane are toxic to insects which are relatively unaffected by dusts or suspensions of this insecticide.

The oil solvents available as insecticide carriers, whether vegetable or mineral, have the following characteristics in common: they are relatively apolar and lack free reactive groups; they are virtually insoluble in water and do not dissociate. In these solvents the lipophilic insecticides readily dissolve, whereas they generally show very little solubility in water. Therefore a study of the effect of these oils and fat-solvents on cuticle permeability may be expected to indicate how the insecticide itself penetrates, or how the solvent carries it through, or how the solvent so alters the cuticle that the insecticide passes through. Essentially this problem is concerned with the lipoid layer of the epicuticle.

It has been discovered that kerosene, which penetrates the cuticle of *Calliphora* larvae only slowly, so alters its structure that a polar compound such as ethyl alcohol can penetrate rapidly, swelling the larvae until they burst.[59] This phenomenon has been interpreted as indicating that the kerosene enters the lipoid layer of the epicuticle and becomes incorporated into it, much as the apolar "tails" of capillary-active substances penetrate surface films of lipoids spread on water in which they are dissolved. Consequently the lipoprotein layer becomes more permeable because of an "increase in free volume and decrease in functional viscosity." The requirement of carrier activity in an oil is that it be apolar. Cyclohexane and methylcyclohexane are as good as kerosene, whereas benzene, toluene, and xylene are inferior. Among the paraffins the best carriers are found in the range between hexane and dodecane, falling off with medicinal paraffin because it is too viscous.[61]

Observations made on the flea showed that carriers such as xylene, medicinal paraffin, and olive oil had the effect of drawing out droplets of water from certain parts of the epidermis; when ethyl alcohol was added to the carrier, this "effervescence" at the body surface was magnified, since the water pulled the alcohol out of the oil to augment the aqueous droplets. It is postulated that here also the carrier disintegrates the lipoid epicuticle and that polar substances draw out the water.[158] The effect of the

kerosene has been interpreted as the removal of lipoid from its normal structural combination with protein in the lipoprotein mosaic of the cuticle.[61] The same result may be obtained with chloroform and even with its vapour.[5]

In this way treatment of the cuticle with apolar carriers allows polar compounds to penetrate, provided they are not too highly dissociated. Thus kerosene will aid the penetration of alcohols, ketones, fatty acids, amines, or phenols.[61] The degree of facilitation of permeability is best measured on the living insect as the speed at which a particular physiological response is elicited, or the reciprocal of the time elapsed between initial contact and final response.

Certain aliphatic alcohols and fatty acids may contain sufficient apolar material in their "tails" to give them a carrier effect to aid their penetration in spite of their polar "heads." When the speed of penetration was measured on *Calliphora* larvae, butyl and amyl alcohols were found to have carrier activity, whereas the higher alcohols were too surface-active to be effective in this regard. Similarly there was a sharp rise in penetrating power with caproic and heptylic acids; the lower fatty acids are strongly reactive and probably have a hydrolytic effect on the cuticular protein.[61] However, it must be mentioned that histological examination showed acetic and butyric acids to be the only members of the series which gave evidence of penetrating the body wall of *Blattella*,[illegible] and that the rate of penetration of isolated cuticle of *Periplaneta* decreased as the series was ascended from methyl to butyl alcohol.[91]

Oil solvents. The efficacy of mineral oils as carriers for pyrethrins through the cuticle of *Rhodnius* has been determined by observing the elapsed time to the development of complete paralysis (Table 4). The penetration of pyrethrins is most rapid when they are dissolved in oils of the lowest boiling point and lowest viscosity. The slow penetration of medicinal paraffin and the refined heavy paraffin P31 has also been noted when they were used as carriers of rotenone or nicotine applied to *Rhodnius*. Determinations performed on the isolated pronotum of *Periplaneta* showed that a thin petroleum oil (b.p. 100–150° C) penetrated over 4 times as fast as a highly refined kerosene (b.p. 200

255° C).[91] However, a light grade of kerosene (b.p. 150–200° C) gave slow partial knockdown of houseflies where a heavier grade (b.p. 190–270° C) gave complete knockdown in 3½ min. This difference bore no relation to the refinable impurities in the two oils and was so great that the lighter oil with pyrethrins added showed no greater knockdown effect, and less toxicity, than the heavier oil.[119]

TABLE 4. Rate of Penetration of Pyrethrins into *Rhodnius* [159]

Oil	Boiling Point	Time to Paralysis
White spirit	150–200° C	2 hr
Odourless distillate	200–260°	4 hr
A12	260–360°	6 hr
P31	320°	6–28 hr
Olive, castor, or sesame oil		$1\frac{1}{2}$–3 days

The vegetable oils afford a considerably lower rate of penetration of pyrethrins in *Ornithodorus* [121] as well as *Rhodnius*. Pine oil penetrates isolated roach cuticle very slowly.[91] Nevertheless free fatty acids, particularly oleic acid, increase the rate of penetration when they are added to the heavy oils.[159] It has also been observed that oleic, linoleic, and coconut fatty acids are effective in increasing the permeability of *Rhodnius* cuticle to transpiration.[158]

A very extensive analysis of the effect of the solvent on the rate of penetration by the dissolved insecticide has been made on the sheep ked *Melophagus*, using the time elapsed to death as an index.[153] The insecticide employed in the experiments was diphenylamine, because it showed a good range of solubility in the various solvents; similar results were, however, obtained with rotenone, dixanthogen, or nitrostyrene bromide. The results tabulated in Table 5 show that liposolubility, as measured by the penetration of the compound into beeswax (representing the epicuticular lipoid), does not give the full measure of a carrier, although it may be a limiting factor, as in the case of aniline or carbitol. A number of other compounds, anisole for example, are found to be ineffective as carriers despite their high liposolubility.

TABLE 5. CHARACTERISTICS OF SOLVENT AS RELATED TO SPEED OF KILL,[153] USING DIPHENYLAMINE AS THE INSECTICIDE AGAINST *Melophagus ovinus*

Hours Elapsed to Kill	Solvent	Beeswax Penetration	Partition Water/Wax	Enhancement of Water Solubility
25–30	Alone	....	....	....
1–5	*o*-Cresol	High	High	High
1–5	*m*-Cresol	High	High	High
1–5	Xylenol	High	High	High
2–5	Benzyl alcohol	Medium	High	High
2–5	*p*-Cresol	High	Medium	Medium
4	Octyl alcohol	High	Medium	Medium
5	Methylcyclohexanol	High	Medium	High
6	Quinoline	High	High	Low
8	Cyclohexanone	High	High	Low
13	Diacetone alcohol	Medium	High	High
17	Cyclohexanol	High	High	Medium
22	Acetophenone	High	Nil	Low
23	Benzonitrile	High	Nil	Low
24	Aniline	Low	High	Medium
24	Carbitol	Low	High	High
27	Dimethylaniline	High	Nil	Nil
27	Methyl benzoate	High	Medium	Low
26	Castor oil	Nil	Nil	Nil
27	Anisole	High	Low	High

It has been postulated that for an insecticide to enter through the cuticle it must not only be lipoid-soluble in the epicuticle, but also have the capacity to pass therefrom into the inner aqueous phase of the endocuticle. In other words it must have sufficient water solubility to ensure that a toxic dose can pass from the wax to the water phase of the endocuticle and body fluids.[158] This capacity is measured as the water/wax partition coefficient and may be determined by shaking the insecticide in a mixture of molten beeswax and water and calculating the ratio of the concentrations in either phase after cooling.

The partition coefficient of the solvent is itself of great importance. If it can readily pass from the epicuticle to the watery endocuticle, it will leave the insecticide the more concentrated in the wax-solvent mixture which then constitutes the lipoid layer. Thus the insecticide in its turn, following its own partition coefficient, will be carried over into the endocuticle. Diacetone alco-

hol, which has mediocre liposolubility but a favourable partition coefficient, enhances penetration much more than anisole, which although highly liposoluble has a negligible tendency to enter water from wax. A further advantage in a solvent is its ability to render the aqueous phase the more soluble for the insecticide; on these grounds methylcyclohexanol is superior whereas methyl benzoate is deficient. The cresols and xylenol, which have a high water/wax partition coefficient as well as high liposolubility, show the highest all-round properties for effective carriers of contact insecticides.[153]

Detergents. These wetting agents are used to increase the spreading power of spray liquids and to enable wettable powders to disperse readily in water. Many detergents also play a part in making these sprays more active by direct contact on the insect. For example, a cetyl ether of polyethylene glycol (R2211) enables rotenone to show contact toxicity to *Rhodnius*, whereas medicinal paraffin, a solvent of similar viscosity, leaves rotenone quite inactive. Solutions of nicotine in this detergent kill by contact in half the time taken by medicinal paraffin solutions.[162]

Application of these cetyl ethers or sodium cetyl sulphate to the dorsal cuticle of *Rhodnius* has the effect of increasing the transpiration rate 3–25 times.[162] It has been found that detergents disrupt not only the lipoid layer of the epicuticle, but also the protein layers of the endocuticle.[114] Comparison of the physical properties of detergents with their contact action show that the most effective properties are (i) enough liposolubility to penetrate and emulsify the epicuticular wax, (ii) a sufficient permeability to water, i.e. not excessively lipophilic, and (iii) the ability to penetrate the outer cement layer of the epicuticle when it is present.[7] The cetyl ether of polyethylene glycol (CO9993) is the most effective detergent that has yet been tested, its superiority to R2211 being a consequence of its greater permeability to water.[162]

Penetration of inorganic lipoid-insoluble poisons

Cuticular penetration may be achieved by not only the lipoid-soluble components of derris and pyrethrin powder, but also the lipoid-insoluble powders of sodium fluoride, borax, and the ar-

senicals. If a cockroach such as *Periplaneta* or *Blatta* runs through sodium fluoride or borax, the powder will be taken up on its legs and belly and eventually will be carried by the cuticular grease to the thoracic sternites between the legs. In the act of cleaning, the roach will ingest this poison by mouth and will die within a day. If the insect is prevented from taking this oral dose by a broad collar attached around its neck, it will nonetheless die within the day with fluoride but will survive for 2–10 days with borax.[127]

Similar results have been obtained with the cricket *Anabrus*, which may be killed by contact application of sodium metarsenite dust. When it is applied along with 3 parts of hydrated lime, the insect is rapidly paralysed and dies within 12 hr. The speed of paralysis and death is no less when the crickets are fitted with collars than when they are allowed to clean themselves, except that the oral dose induces regurgitation and defaecation. Contact poisoning may be obtained without the lime. It has been observed that the toxicity and speed of kill with these contact dusts are greater at higher humidities.[49]

It has been found that arsenites may penetrate the cuticle of the locust *Schistocerca*, since death occurred 10–11 days after application to the metanotum or other sclerotized parts. Application to antennae or intersegmental membranes resulted in death after a considerably shorter period. Again it was noted, for Paris green as well as arsenites, that the speed of action was increased at higher humidities.[71]

If arsenious oxide or sodium arsenite is affixed to the dorsal metathorax of *Periplaneta* in capped wax cells, absorption of arsenic may be detected in the body by chemical means. Both arsenicals were found to absorb water from the cuticle. Sodium arsenite absorbed more water and was absorbed itself into the body 4 times as fast as arsenious oxide. The rate of absorption of arsenic was a function of the amount of cuticle surface exposed.[92]

Studies on contact dusts of sodium fluoride showed that no penetration occurred *via* the antennae of *Periplaneta*, but that paralysis and death resulted within 12 hr if the powder was placed between the legs, particularly behind the metacoxae.

Mortality also resulted from application to the ventral surface of the abdomen, but not the dorsal.[52] The speed of paralysis was greatly increased by pretreatment or simultaneous treatment of the cuticle with lime. Presumably this induced a saponification of the epicuticular grease, since a subsequent application of oleic acid was found to cancel the effect of pretreatment with lime.[53]

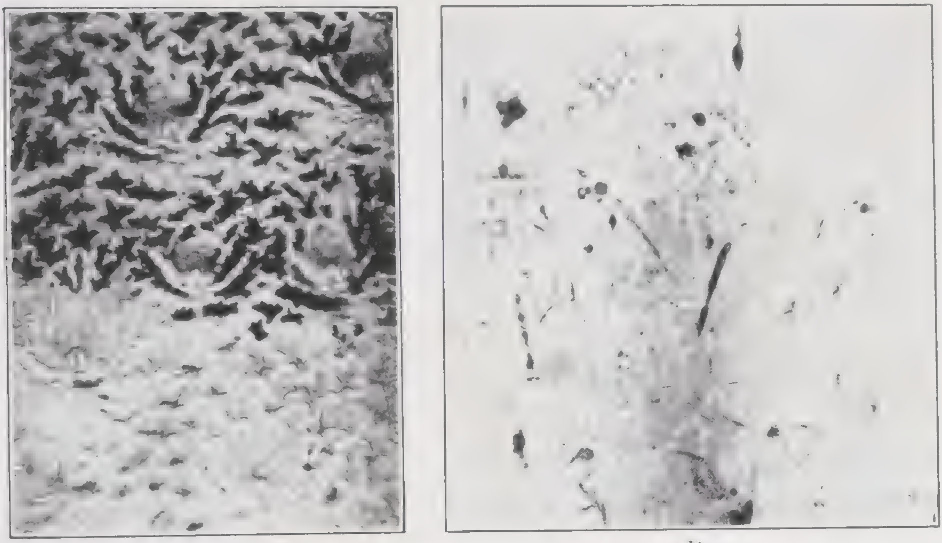
The action of inert dusts on cuticle

An ancient but effective means of controlling insects by contact was the application of soot, ashes, or road dust. Further refinement has led to the use of activated charcoal, the oxides and carbonates of magnesium and calcium,[143] the siliceous minerals, and finely powdered alumina. These applications are ineffective at 100% relative humidity, but their efficacy increases with increasing dryness of the atmosphere. Their mode of action involves withdrawal of body water from the insect. When the material is hygroscopic, such as soot or activated charcoal, this is effected by the direct adsorption of water on the dust. When the material is non-hygroscopic but abrasive, such as pyrophyllite or alumina, the action involves a laceration of the waterproof layer of the cuticle, allowing moisture to be lost to the surrounding air. Indeed the insecticidal activity of a dust material has been found to be proportional to the amount of cuticular abrasion and weight loss that it engenders in the insect.[20a]

It has been discovered that these inert dusts can mop up, by crystalline attraction, the outer layers of wax or grease on the surface of the epicuticle. The inner molecular layers of epicuticular lipoid which are oriented by attraction to the underlying protein are resistant to this process unless they are disrupted mechanically.[5]

This disruption is effected by the insect's own movements, where they result in rubbing the abrasive dust over the epicuticle. The bug *Rhodnius*, dusted with powdered alumina, will not dry up if it is protected from rubbing; but if it is allowed to rub its abdomen on the walking surface it will dry up in a day. That the lipoid layer has been removed from the ridges of the epicuticle may be demonstrated by the reduction of ammoniacal

silver hydroxide at those spots by the polyphenols of the exposed endocuticle[160] (Fig. 8).



A B

FIG. 8. Surface view of insect cuticles treated with ammoniacal silver and hydrogen peroxide to show abrasion. A. *Rhodnius* nymph; lower half normal, upper half rubbed with alumina dust. B. Ventral surface of third abdominal segment of a wireworm. (From Wigglesworth, 1945)

The insect *Rhodnius* responds to abrasion by the migration of hypodermal cells to the affected areas, and the regeneration there of a soft waxy bloom. Since this resecreted wax lacks the usual covering of epicuticular cement characteristic of this species, any dust still remaining on the body surface will readily mop this wax up also. Or if the insect is in dry air, it may die of desiccation before sufficient new wax has been secreted to waterproof it.[158]

This abrasion will also facilitate the cuticular entry of contact insecticides. A preliminary rubbing with powdered alumina has been found to reduce the time required to kill *Rhodnius* by a given contact dose of rotenone powder from 3 weeks to 1 day, or the time required for paralysis with aqueous nicotine from 24 hr to as little as 20 min.[158] As a practical application it has been discovered that dilution of rotenone with an abrasive dust such as pyrophyllite increases its effectiveness against *Leptinotarsa*, *Epilachna*, or *Pieris* by 3–5 times.[146]

Insects inhabiting the soil show scratches on the cuticle which have been presumably produced by the abrasive action of soil particles (Fig. 8). In cutworms they are most frequent on the lateral folds, while with white grubs they appear on the dorsum also. The rate of water loss from a wireworm larvae has been determined to be proportional to the number of cuticular scratches.[161] The cuticular penetration of arsenicals in the wireworm *Limonius* probably takes place at these abraded areas.[170]

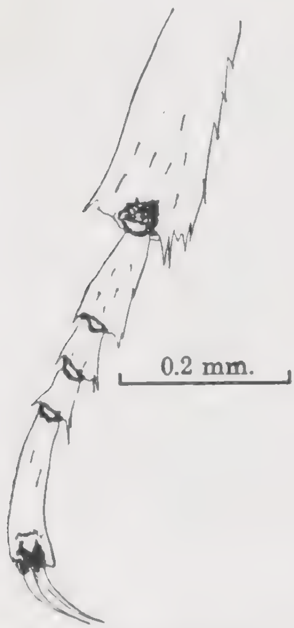


FIG. 9. Abrasion of joints of metathoracic tarsus of *Tribolium* by alumina dust. (From Wigglesworth, 1947)

Even insects inhabiting wheat flour become slightly abraded with advancing age. If powdered alumina is added, which is an excellent control measure, it will be found that active species such as *Tribolium* or *Sitophilus* become more abraded than a sluggish insect such as *Anobium*.[163] The abrasion occurs mainly at the joints of the legs (Fig. 9). The specialized cuticle of the larva of the dipterous *Calliphora*, where the proteinoid epicuticle has an exceedingly thin lipoprotein layer, is neither abraded by nor adsorbed onto dusts as abrasive as silica or silicon carbide (*Carborundum*).[23]

Penetration of materials into the egg

The outer covering of the egg, the chorion, is secreted by the follicular cells of the mother. The thick exochorion consists of lipoprotein, while the thin many-layered endochorion is protein in nature. It would appear that penetration, in the cases where it occurs, takes place through the minute pores present in the chorion of some eggs, or through the thin region at one end known as the micropyle. In eggs of *Epilachna*, *Anasa*, and *Chrysopa*, whose chorions are porous, petroleum oils were found to penetrate easily to produce a layer within the chorion. In *Oecanthus* and *Dilachnus*, which lack conspicuous pores in the chorion, penetration appeared to be confined to the region of the micropyle.[88] In

eggs of *Aedes aegypti*, no penetration of petroleum oils at all could be detected through the tough chorion.[102]

Careful work performed with the eggs of *Rhodnius* showed that permeability was confined to the 15 or so micropyles on the rim of the shell under the cap. In eggs laid by young females these were sealed with a cement of tanned protein. The chorion was underlaid by a wax layer. Aqueous solutions penetrated the outer lipophilic portion of the micropyle very slowly, replacing the air normally filling it, to reach and pass the inner hydrophilic portion and the wax layer. Oils which passed the cement more rapidly were successful in penetrating the micropyle, and those which were wax solvents disrupted the wax layer and thus proved to be toxic ovicides.[6]

Aphid eggs are also known to be resistant to petroleum oils, and for ovicides recourse has been taken to tar oils and derivatives of phenol and cresol such as DNOC.[58] The action of phenol has been found to involve the softening and eventual disintegration of the chorion of *Aphis*. Acetic acid and other corrosives slowly penetrate the chorion of *Rhodnius*.[6] Lime-sulphur, on the other hand, hardens the chorion and the embryo within dries up.[97] It has been suggested that this hardening may interfere with the permeability of the chorion to the gaseous exchange of the egg.[58]

Deeper entry into the egg involves the penetration of the vitelline membrane, which is secreted by the serosa cells of the egg itself, and which contains a chitinoid substance overlaid with a waxy hydrophobic layer similar to cuticulin. In *Epilachna* the petroleum oil which passed the chorion was observed to spread over this membrane without penetrating it; in *Chortophaga* the oil followed along the folds of the embryo, presumably because it could not penetrate further. In *Anasa* the oil penetrated into the interior of the egg but largely avoided the embryo itself; in *Periplaneta* streaks of oil extended to the centre of the embryo. In *Oecanthus*, *Dilachnus*, and *Chrysopa* the oil collected around the fat globules of the yolk. This deep penetration involved exposure of eggs to the oil for 48–96 hr.[88]

There is evidence, however, that petroleum oils may exert their lethal effect, which is more properly regarded as an inhibition of hatching, without penetrating the chorion at all. Eggs of *Aedes* are killed without any oil being found within the shell.

The eggs of the European red spider fail to hatch after treatment with summer oils, although the oil does not penetrate the chorion. There is no inhibition of embryonic development, and it appears that hatching is prevented by the oil having made the chorion tougher.[68] The petroleum oil that inhibits the hatching of *Grapholitha* eggs may be removed by rapid rinsing with pentane or ether, indicating that it cannot have penetrated below the surface of the egg. The action of this highly refined paraffin oil depends on the duration of the dosage rather than its intensity. If the oil were removed within 5 hr of its application, the percentage hatch was only slightly reduced no matter how heavily the oil was applied; whereas a light application kept on the egg for 24 hr killed 95%, provided that it exceeded the threshold level for toxicity. The initial effect of the oil was to depress the respiratory rate by as much as 80% in the first 2 hr, which subsequently rose slightly to a reduced base-level which might continue beyond the point at which hatching was normally due.[131]

Since eggs of *Grapholitha* failed to hatch when confined in a small volume of air to which oxygen was added and from which the CO_2 was constantly removed, it appeared that they must produce some gaseous toxic metabolite. It was therefore suggested that petroleum oils exerted their effect by constituting a surface envelope through which the egg could not rid itself of toxic metabolites.[131] With *Aedes* eggs, it was concluded that oils exerted their effect by preventing the entry of oxygen rather than the escape of toxic gases. Whereas the mortality in an atmosphere of nitrogen or hydrogen was 80–98%, and with carbon dioxide 50%, in pure oxygen all the eggs hatched.[102]

However, in some cases petroleum oils may not constitute a barrier for the penetration of enough oxygen to satisfy the needs of the egg. The parasite *Habrobracon* can hatch under a covering of medicinal paraffin as well as in its natural state on the cuticle of a caterpillar. If, however, the egg is confined in a small volume (0.05 cc) of the oil, which in turn is sealed from the outside air, it will invariably fail to hatch. Thus it may be concluded that normally paraffin oil allows sufficient exchange of the respiratory gases of *Habrobracon* eggs.[106]

Wetting and spreading of liquids on the cuticle

The cuticle of most terrestrial insects, because of its surface layer of fatty material, grease, or wax, has little affinity for water and is described as hydrophobic. Thus when aqueous solutions are applied they fail to wet the cuticle and spread over it, but gather themselves into droplets and roll off the insect. This inability to wet the cuticle is enhanced by hairs, spines, and microtrichia, which trap pockets of air between the aqueous liquid and the cuticle, preventing its being wetted at all. Once contact has been established, the degree to which the liquid applied spreads over the cuticle depends essentially on the degree of adhesion or molecular affinity between the liquid and the layer of solid material on the surface of the cuticle.

The degree of adhesion may be measured as the amount of work which must be performed to separate the two phases. This is proportional to the difference between the free energy associated with the new state (that of the solid and liquid separated, $\gamma_S + \gamma_L$) and the free energy of the original state (that of the interface, γ_{SL}). It may be expressed as the surface tension of the liquid (T_L) added to the surface tension of the solid (T_S) and reduced by the amount of the interfacial tension (T_{SL}) between the liquid and the solid.[1,9a]

$$W_A = T_S + T_L - T_{SL} \tag{1}$$

Of these quantities, T_S (the surface tension of the solid epicuticle) and T_{SL} (the interfacial tension) cannot be determined in practice. However, the amount of adhesion (in terms of the work necessary for separation) may be established, knowing only the surface tension of the liquid applied, by measuring the angle which the edge of the liquid droplet makes with the plane surface of the epicuticle,[1,165] viz:

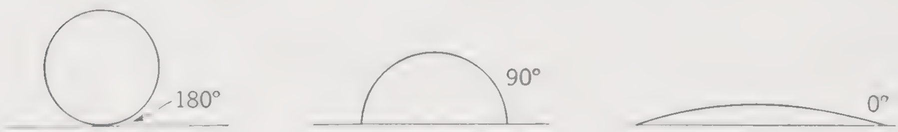
$$W_A = T_L(1 + \cos\theta) \tag{2}$$

θ is described as the contact angle and is measured as the advancing angle while the droplet is still spreading. The two equations may be combined to represent the surface energy equilibrium existing when the droplet has spread to show a given contact angle:[58]

$$T_S = T_{SL} + T_L \cos\theta \tag{3}$$

The function $T_L \cos \theta$, which represents the energy available per unit area of interface, can thus be measured for the liquid-solid system concerned. It is expressed in ergs per square centimeter and is termed the adhesion tension.[89]

Where the contact angle approximates 0°, the liquid has as much attraction for the solid as for itself, and it will spread as far as the number of molecules in the liquid droplet allow. If the contact angle approximates 180°, there is no adhesion between the liquid and the solid, and the liquid will gather itself into a spherical droplet as dictated by its own surface tension.



A contact angle of 90° indicates that the liquid has half as much attraction for the solid as for itself. The liquid will stay on the solid, will "wet" it, but its spread will proceed only as far as a right-angled contact angle will allow. Thus some writers consider wetting to have occurred only if the contact angle is less than 90°; however, in the strict sense wetting or adhesion must have occurred even when the angles exceed 90° and the droplets have overhanging margins, otherwise the angles would not have been there to measure, despite the fact that the droplets later roll off with the slightest movement of the cuticle.

The fate of contact sprays on the insect cuticle has been interpreted to involve (i) wetting, or molecular adhesion of liquid to solid, excluding any intervening air, and (ii) spreading, which occurs if the affinity between liquid and cuticle is greater than the affinity of the liquid molecules for themselves (measured as the liquid surface tension T_L).[83] Any reduction that is effected in T_L will increase the ability of the liquid to spread and reduce its contact angle with the solid. The surface tension of water (76 dynes/cm) is too high for spreading to occur on the wax of the insect cuticle, but if it is reduced by the addition of soap, saponin, or a sodium alkyl sulphonate, the contact angle will be sufficiently reduced to allow wetting and spreading to occur (see Table 6).

TABLE 6. ANGLES OF CONTACT OF LIQUIDS APPLIED TO INSECT CUTICLE[5]
Advancing angles, measured in degrees

Species	Distilled Water	0.5% Aqueous Solutions of Sodium Oleate	Penetrol *	Saponin
Aphis rumicis (A)	180	67	94	68
Musca domestica (A)	180	22	106	117
Blattella germanica (A)	180	23	62	70
Tenebrio molitor (L)	180	40	72	91
Pieris rapae (L)	180	51	67	106

* Sodium salt of petroleum sulphonic acids, avg. C_{16}.

This table shows the effectiveness of sodium oleate (hard soap) in enabling aqueous sprays to wet and spread upon the insect cuticle. The surface tension of 0.5% sodium oleate is 28 dynes/cm, as compared with 76 for distilled water. Saponin is seen to be less effective than soap as a "wetter and spreader." Kerosene, also with a surface tension of 28 dynes/cm (see Table 7, p. 214), has no difficulty in spreading on cuticle, like most oils of low viscosity. The percentage kill of California red scale was found to be correlated with the concentration and effectiveness of the spreading agent. Aqueous solutions of spreaders have a much smaller contact angle on the wax of these insects than on leaf wax; and sodium oleate, although the best spreader for scale wax, is surpassed by other compounds in spreading on *Viburnum* foliage.[31a] It should be noted that nymphs of the whitefly (*Psylla pyrisuga*), for example, exhibit a contact angle of less than 40° with pure water, because of the incrustation of their cuticle with hydrophilic carbohydrate.[58] In comparing several species of insects with lipophilic epicuticles, it has been found that the more solid their epicuticular wax, the more resistant they are to the spreading action of contact sprays; there is a direct correlation between the melting point of the wax and the contact angle of aqueous solutions.[5]

The rate of spreading is dependent upon the viscosity of the liquid, but the extent of spreading is dependent upon its surface tension T_L, to which it bears an inverse relationship. For instance a 2-cu-mm droplet of 1% sodium oleate in water (s.t. 28.4 dynes/cm) will spread on the bee cuticle sufficiently to cover 14 sq mm, whereas a similar droplet of pure water (s.t. 76 dynes

cm) will cover only 2.5 sq mm. As a measure of the spreading power of a liquid applied to a solid, use has been made of the spreading coefficient originally derived to characterize the spreading of surface films on water. It is equivalent to the work of adhesion minus the work of cohesion:

$$S = W_A - W_B \tag{4}$$

The work of cohesion, W_B, of the applied liquid is equivalent to twice its surface tension. When it is subtracted from W_A, for whose calculation see above, a negative value will result. The equations concerned are as follows:

taking $W_A = T_S + T_L - T_{SL}$ (equation 1), then

$$S = T_S - (T_L + T_{SL}) \tag{5}$$

taking $W_A = T_L(1 + \cos\theta)$ (equation 2), then

$$S = T_L(\cos\theta - 1) \tag{6}$$

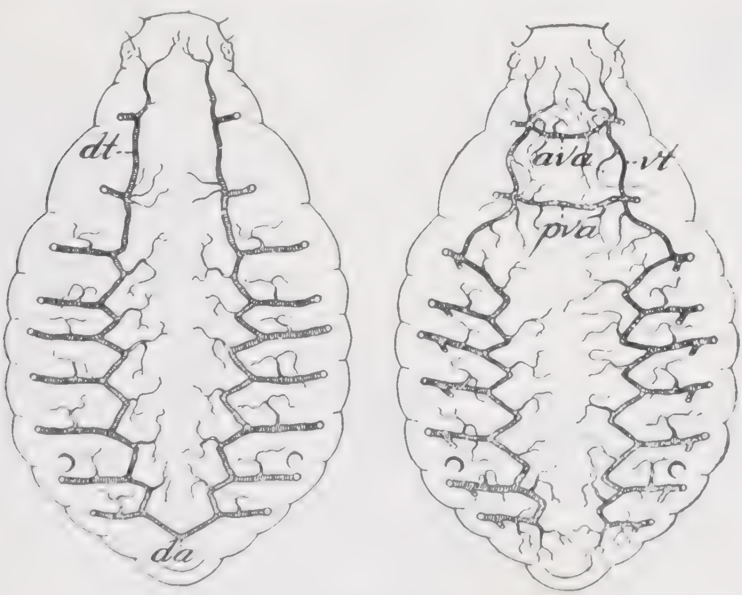
Thus all spreading coefficients are negative, tending towards zero as the contact angle decreases to zero. For instance, the spreading coefficient of 0.1% nicotine in distilled water was found to be −81, whereas in 0.5% sodium oleate it was −2.9. The raising of the spreading coefficient S from −81 up to −2.9 allowed the sodium oleate solution to spread.[165] Had it been reduced to zero, the contact angle would have been zero and the spreading would have continued as far as the number of molecules in the applied material would allow.

From examination of equation 5 it will be seen that the spreading coefficient is greater (i.e. less on the negative side) the lower the values of T_L and T_{SL}. Thus a reduction in the interfacial tension T_{SL} will also increase spreading, besides increasing adhesion (W_A) as shown in equation 1. Indeed it has been found that most wetting agents reduce the interfacial tension (T_{SL}) as well as the surface tension (T_L). This may be visualized as a slight solubility of the liquid in the solid surface, which reduces the interfacial tension, until if they are entirely mutually miscible T_{SL} has decreased to zero. Certain detergents reduce the surface tension without affecting the interfacial tension, and it must be due to this fact that saturated solutions of nonylic acid, despite a T_L as low as 38 dynes/cm, show no greater spreading power on insect cuticle than distilled water. On the other

hand, the increase of the concentration of soap solutions increases their spreading power, despite a failure to show any further fall in T_L, presumably because they reduce the interfacial tension T_{SL}.

Tracheal penetration

Except for the simplest forms, which breathe through the cuticle, the respiratory processes of insects are carried out by tracheae. These air-filled tubes ramify through the body, breaking up into smaller branches and ending in the tracheoles, which enter and aerate the muscle and nerves (Fig. 10). The tracheae open to the exterior at the spiracles, of which there may be a pair in almost every segment (e.g. orthopterans, caterpillars) or which may be restricted to a total of one or two pairs (e.g. dipterous larvae, scale insects). The spiracles often exhibit sunken or tortuous entrances which may contain valves or sphincters or be closed by lips or opercula (Fig. 11).[81] Before ramifying into the tissues, the tracheae usually lead into longitudinal tracheal vessels, which may be greatly swollen to form air sacs in insects like the fly or the bee.



A B

FIG. 10 Diagram of tracheal system of an aphid. A. Dorsal system: *dt*, dorsal trunk; *da*, dorsal arch. B. Ventral system: *vt*, ventral trunk; *ava* and *pva*, anterior and posterior ventral arches. (From McIndoo)

Where the spiracles are sunken, the walls of the spiracular atria are lined with the same layers as the outer integument, which are renewed at each moult.[154] The tracheae are thickened with interior rings or helices called taenidia, which have the effect of strengthening them against collapse. The tracheal wall, as has been found in *Periplaneta* and *Phormia* larvae, is composed of chitinous microfibres set in an extremely thin continuous membrane, 0.01–0.02 μ thick, in which no holes or pores have been detected. Oddly enough the tracheal walls in adult *Phormia*, *Musca*, or *Apis* have proved not to show the properties of chitin.[14] In the taenidia the microfibres of chitin are directed around the circumference of the trachea and are thus arranged at right angles to their lengthwise alignment in the intertaenidial membrane.[114] The membrane may be either uniform or reticulate in structure or more often it exhibits scattered minute excrescences.[113] The tracheoles are of very small diameter, from 0.5 μ down to 0.2 μ at their termination in the tissue cells.[114] Their membranous wall is only 0.005 μ thick, in which no pores are discernible by the electron microscope;[110] nothing is known of its chemical composition.

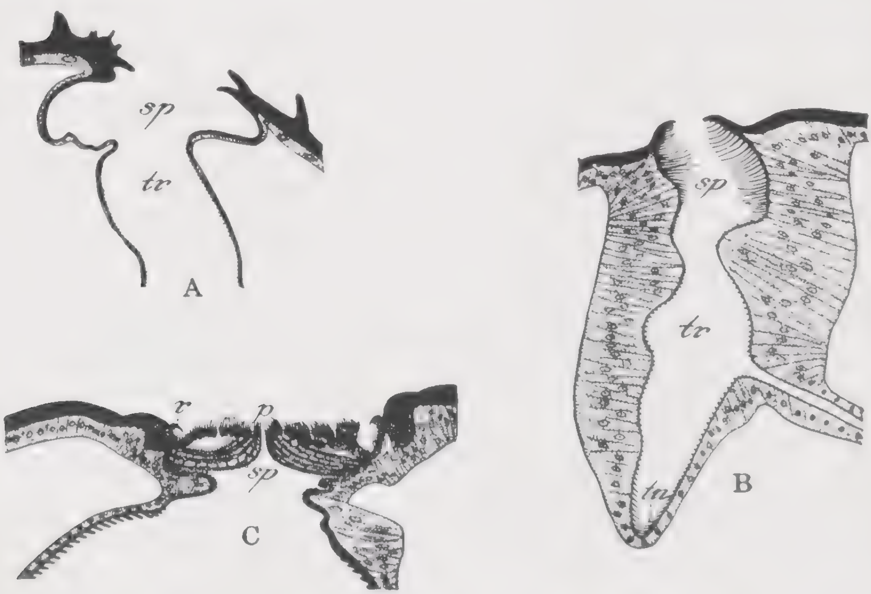


Fig. 11. Types of spiracular closure. A. *Orthezia insignis*, ×500. B. *Atteva aurea*, ×190. C. *Phlegethontius sexta*, ×50, showing the closing plate. (From McIndoo)

Water and aqueous solutions and suspensions of insecticides, having high surface tension, are unable to enter the tracheae.[83] But mineral oils and aqueous solutions of wetting agents, with the surface tension reduced to about one-half that of water, are able to do so. Emulsions may penetrate tracheae, either as the oil fraction after breaking, or as the intact emulsion.[83] The liquid must be able to spread into the tracheae along its walls, following the same physical laws that govern its spread on the cuticle. The adhesion tension, $T_L \cos \theta$, represents the available energy per unit area of surface of the tracheal wall. The capillary pressure, ϵ, which represents the available energy per unit of cross-sectional area of the trachea,[88] is represented by:

$$\epsilon = \frac{2T_L \cos \theta}{r}$$

A similar formula governs the height, h, of ascension in a capillary tube:

$$h = \frac{2T_L \cos \theta}{r}$$

from the relationship $T_L \cos \theta = rdgh/2$, in which d (the density of the liquid) and g (the acceleration due to gravity) may be disregarded since they are constants.[83]

By analogy with the spread of liquids on the cuticle, energy is available only if the angle of contact is less than 90° and $T_L \cos \theta$ is positive. For angles of contact in excess of 90°, the capillary pressure is negative since $\cos \theta$ is a minus value. Thus only those liquids which show contact angles of less than 90° can penetrate, and their penetration will continue, provided the properties of the tracheal wall farther inside the insect do not change to increase the angle of contact.

The technical difficulties involved have prevented any systematic measurement of contact angles in tracheae. Thus the relationship between the surface tension of a liquid and its power of tracheal entry remains on an empirical basis. Contact-angle measurements made on the cuticle are of assistance only in a very rough way and are apt to be misleading; for whereas the angle made by 0.5% sodium oleate with the cuticle of *Phlege-*

thontius was 29°, indicating strong spreading properties, the angle found as the sodium oleate advanced into a trachea was 85°, indicating a weak capillary pressure.[165] The empirical relationship between the surface tension of sprays and their tracheal penetration into adults of *Apis* and larvae of *Phlegethontius*, *Pieris*, or *Tenebrio* is shown in Table 7.

TABLE 7. Surface Tension of Aqueous Contact Sprays and Their Penetration into the Tracheal System

Material	Surface Tension, dynes/cm	Tracheal Penetration	Species
Distilled water	76	None	*Apis* [79]
0.1% Nicotine	68	None	*Phlegethontius* [165]
1% Nicotine sulphate	53	None	*Pieris* [79]
0.5% Ca caseinate	52	None	*Phlegethontius*
1% Saponin	42	None	*Pieris*
0.5% Penetrol	39	Good	*Phlegethontius*
Sat'd Nonylic acid	38	None	*Apis*
15% Na caproate	35	None	*Pieris* and *Tenebrio* [89]
0.05% Na oleate	27	Slight	*Pieris* and *Tenebrio*
0.5% Na oleate	23	Good	*Phlegethontius*
0.5% Na oleate	28	Good	*Pieris* and *Tenebrio*
1% Na oleate	29	Very good	*Pieris* and *Tenebrio*
1% Na oleate	28	Good, slow	*Apis*
3% Na oleate	31	Very good	*Pieris* and *Tenebrio*
Kerosene, white	28	Good, rapid	*Apis*

It was concluded that for entry of the propodial spiracles in *Apis*, the surface tension of the spray liquid should be below 40 dynes/cm,[79] and for tracheal penetration in *Pieris* or *Tenebrio* it should not exceed 35 dynes/cm.[89] In experiments on *Aphis* it was found that solutions of *Penetrol* with surface tensions up to 39 dynes/cm could enter the tracheae.[165] Solutions of saponin, gelatin, or calcium caseinate did not allow tracheal entry in *Aphis*, even though their surface tension was well below this figure; these materials do not wet the insect thoroughly. Solutions of saponin and gelatin exhibit surface viscosity and rigidity because of the tendency of their molecules to crowd into interfaces, and emulsions containing them have been observed to roll off the insect cuticle. Solutions of nonylic acid, though of a low surface tension, will not spread on the cuticle of *Apis*.[79] An

increase in tracheal penetration of *Pieris* and *Tenebrio* was obtained when the concentration of sodium oleate solutions was raised from 0.05 up to 3%, and their ability to spread on the cuticle of *Apis* was also increased. Measurements of the static surface tension of these solutions show no decrease as the concentration of soap is increased.[89] This is a consequence of the measurement being made at the solution surface, where the soap molecules congregate to produce the same high concentrations whatever the percentage in the general solution. The greater spread with the higher concentrations of soap is due to a decrease in the interfacial tension with the cuticle and tracheal wall; for example, increasing the concentration of sodium oleate from 0.04 up to 2% decreases its interfacial tension with *Vaseline* from 30 down to 1 dyne/cm.[17] These findings suggest that high concentrations of this soap exert a direct effect on cuticle and tracheal wall, which results in a decrease of interfacial tension.[79]

Although the adhesion tension $T_L \cos\theta$ indicates whether or not tracheal penetration can occur, and how much energy is available for it, it offers no measure of the speed of penetration. This is represented by the penetrativity of the liquid, expressed by the adhesion tension divided by twice its absolute viscosity:

$$\text{Penetrativity} = \frac{T_L \cos\theta}{2\eta}$$

Thus liquids having a high adhesion tension but also high viscosity show negligible penetrativity. An example is castor oil, which proves unable to penetrate the tracheae of *Blattella*[83] or to spread evenly on the cuticle of scale insects.[25] Oils of intermediate viscosity are found to penetrate slowly, whereas light oils of low viscosity penetrate quickly. The speed of penetration also varies inversely as the radius of the trachea.[57]

Although kerosene has been observed to penetrate the tracheal system of *Aonidiella* rapidly, it is often pushed out again by respiratory movements, to be lost by evaporation. More viscous material such as refined lube oil, linseed, or cottonseed oil penetrate completely and remain in the tracheal system. Turpentine, oleic acid, and miscible oil penetrate only a certain distance into the system, but remain there.[25] As the oil encounters tracheae

of ever-diminishing calibre its speed of penetration decreases in direct proportion to the diameter of the trachea, so that its advance becomes no longer perceptible. It should be pointed out that the same law governs the reverse process; the further the oil penetrates into the finer branches, the more energy is required to expel it.[57]

It is considered that generally the entry of oils is opposed by the air pressure in the trachea, backed up by hydrostatic pressure of the fluid in the finer branches. Indeed oils which had stopped penetrating into *Aonidiella* have been observed suddenly to advance, as if the trachea had broken and the pressure had been relieved. However, the reverse may occur and penetration be aided by inspiratory currents. The fact that the sodium oleate solution mentioned above can enter the trachea of *Phlegethontius* so readily in spite of only weak capillary pressure would indicate that entry had been assisted in some way, particularly since it did not occur in larvae which had just previously been killed with cyanide.[165] Observations on the penetration of oils into mosquito larvae suggest that tracheal penetration might be aided by reduced pressure in the sections yet unfilled.[156] On the other hand, mosquito larvae may sometimes be protected against entry of oils by the outer tracheae collapsing inwards; the toxic aromatic oils are most liable to cause this effect and thus may kill more slowly than the less toxic aliphatic oils.[86]

Once well within the tracheal system, oils, solutes, and vapours may diffuse into the haemolymph through the walls of the tracheae or tracheoles. The fate of solutions of pyrethrins in oil dyed with gentian violet suggests that diffusion takes place through the walls of the tracheae into the haemolymph and thence to the ganglia of *Periplaneta*.[124] In *Culex* larvae similar dyed solutions have been traced directly to the ganglia by way of the tracheoles which ramify within them. The ability of dyes to penetrate the wall, even those of a molecular weight of approximately 400 (Congo red) and greater, indicates that the permeability of the tracheole wall is not unlike that of a dialysis membrane.[115] Kerosene with dissolved picric acid will penetrate the tracheal wall of *Blattella* to stain the surrounding tissues as well as the walls themselves. Gasoline penetrates the tracheal

walls in liquid or vapour form to dissolve the fat in the surrounding tissues. It is considered that soaps pass the tracheal walls after being first hydrolysed to the fatty acids.[83]

The diffusion of vapours through the tracheal wall is a process probably similar to the penetration of certain gases through membranes of organic polymers, which has already been studied.[1] The penetration of fumigant vapours through the tracheal walls into the surrounding tissues has been followed by trypan blue staining,[83] and in the case of H_2S by testing with lead acetate.[81] A low-vapour-pressure fumigant such as nicotine has been followed into the trachea, the surrounding tissues, the fat body, and the ganglia by testing for the precipitate with phosphomolybdic acid. Droplets of condensed nicotine have thus been detected far within the tracheal system of *Myzus*[81] (Fig. 12).

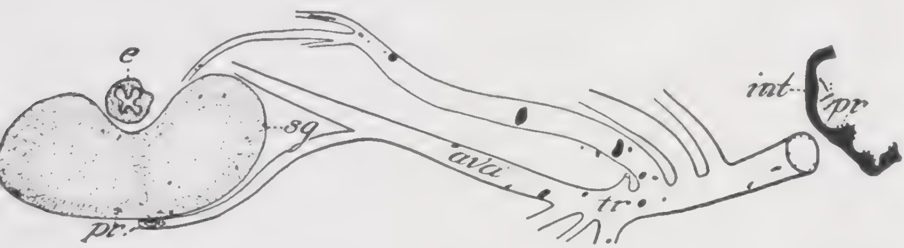


FIG. 12. Penetration of nicotine in tracheae and ganglia of an aphid. *pr*, precipitate with phosphomolybdic acid on outer surface of integument, *int*; in the tracheae, *tr*; and in the suboesophageal ganglion, *sg*. (From McIndoo)

It is surprising to find that insecticidal dusts can enter the tracheae of insects in certain instances. There is evidence that sodium arsenite particles may enter the outer sections of the tracheae of locusts while in flight.[71] Derris dusts have been discovered to enter the tracheae of *Melophagus* and to be carried in the posteroanteral air circulation, a mode of entry more effective than cuticular penetration.[152]

Where contact sprays are concerned, it is difficult to assess the importance of tracheal entry as compared with cuticular penetration, because it varies according to the type of insect and the insecticidal formulation employed. It would appear that flies and aphids are susceptible to tracheal entry, since only by this route can so fast a knockdown be explained, and evidently they

are more susceptible to this mode of entry than the honeybee with its well-developed powers of spiracular closure. It is also apparent that nicotine exerts its fast fumigant effect chiefly by this route of entry. Some insecticides, however, show variation in the principal route, depending on the insect attacked; derris powder, which may kill *Melophagus* by spiracular entry as noted above, can kill *Bombyx* larvae by cuticular entry alone when all the spiracles have been artificially sealed against entry. Some species of insects show variation in the mode of entry, depending on the poison employed; comparison of the speed of death with depth of tracheal penetration in the beetle *Melasoma* showed that the liquid compounds tested fell into two classes: those where a correlation existed and therefore the tracheae were the route of entry, and those where there was no correlation and the mode of entry was presumably by another route.[59]

Entry of stomach poisons *via* the alimentary canal

The main point of entry of stomach insecticides into the system of the insect is the mid-gut or ventriculus, since this is the site of absorption of the digested food and is the only part of the alimentary canal which is not lined with a chitinous intima. Although poisoned food may be held for a long time in the crop of locusts or roaches, or the honey stomach of bees, no absorption occurs in these stomodaeal organs. When nicotine was fed together with indigo carmine to the honeybee, the dye demonstrated that it had been absorbed in the mid-gut, and it could be traced through the haemolymph to certain muscles and the Malpighian tubules; no penetration was detected in the small intestine and rectum, which together constitute the proctodaeal portion.[81] Sodium metarsenite fed to *Periplaneta* was found to be absorbed by the ventriculus into the haemolymph and deposited in the tissues.[35] Analysis of the alimentary canal of roaches and locusts poisoned by arsenicals showed that most of the arsenic had been taken up by the tissues of the mid-gut, with little in the hind-gut and even less in the fore-gut.[35]

The first line of defence an insect has against eating poisoned food is to avoid it on evidence of its odour; in this way housefly maggots may be repelled from the poison coumarin. Yet honeybees are not repelled from deposits of benzene hexachloride that

are highly odorous to man.[141] The factors of olfactory and gustatory repellency do not appear to be the problem in insect control that they are in rodent control.

The second line of defence is to refuse to eat poisoned food in sufficient amounts. Larvae of *Euxoa* and *Euproctis* will avoid eating foliage poisoned with sodium arsenite, although they show no aversion to sodium fluosilicate.[58] Migratory locusts avoid eating food poisoned with sodium arsenite or Paris green, but not with sulphur or calcium caseinate.[150] On the other hand, rotenone is highly toxic to *Bombyx* larvae in spite of inhibiting the ingestion of more food.[37, 168]

Furthermore the poisoned food may be eliminated by regurgitation. The effect of sodium arsenite on *Euxoa* larvae is first to inhibit the normal contractions of the anterior sphincter of the mid-gut and then to throw it into violent spasms which result in vomiting. No such effect is obtained with larvae of *Pieris brassicae*, which do not regurgitate.[149] The addition of digestive sedatives to stomach poisons might be profitable to prevent regurgitation, since bismuth subcarbonate was found to increase the effectiveness of lead arsenate for *Popillia*.[87]

The diarrhoea which is caused by many of the more soluble arsenicals, whether by a plasmolytic effect or by inducing hypersecretion of intestinal fluids, may eliminate the poison too fast for any more than a small fraction to be absorbed.[58] Although sodium metarsenite and Paris green are purgatives for *Euxoa* and *Pieris*, they prove to be the reverse for *Locusta*.[149] And whereas lead arsenate or rotenone decreases the passage time of food through the gut of *Periplaneta*, sodium fluoride or arsenious oxide increases it.[132]

Rotenone may be passed through the alimentary canal of *Prodenia* without any of the poison being absorbed.[168] The same phenomenon has been noted with phenothiazine in the cockroach It is possible that some of the larger poisonous molecules may be withheld by the peritrophic membrane which encloses the food masses in the mid-gut, or alternatively may not enter the epithelial cells. Investigations conducted on a species of termite have shown that dye molecules of the size of Congo red are withheld, yet in *Glossina* molecules as large as those of haemoglobin can diffuse or dialyse through the peritrophic membrane. How-

ever, of the dyes which passed the membrane, only the smallest colloidal ones were found to enter the cells of the mid-gut of *Apis* or *Calliphora*.[21]

Certain species of insects may be able to destroy stomach insecticides which are toxic to their near relatives, or to themselves by contact. The larvae of *Prodenia eridania* can hydrolyse pyrethrins in the alimentary canal and body tissues at a rate sufficient to render them ineffective.[169]

Experiments with sodium arsenite and Paris green showed that *Euxoa* larvae absorbed only a very small fraction of the arsenic in the food, much less than *Pieris* and *Locusta*, and that this fact partially accounted for the higher median lethal concentration required. Whereas between 35 and 40% of the ingested arsenic could be found in the body tissues of *Pieris* and *Locusta*, only 20% could be found in *Euxoa*. The efficiency of the Malpighian tubules in currently removing the absorbed poison was deduced to be also a factor. Whereas with the two susceptible species the arsenic in the body could be increased by implementing the stomach dosage, with *Euxoa* even a tenfold increase in dosage could not increase the amount in the body tissues.[149] When *Periplaneta* was fed sodium metarsenite, only 12% of the arsenic administered was found to be deposited in the tissues before death.[35] When *Tenebrio* or *Phlegethontius* was fed As^{76} as arsenious oxide, little of the radioactive poison was absorbed from the alimentary canal.[85]

The inorganic stomach poisons are applied in as insoluble a form as possible to prevent their being washed away by rain or dew. Yet they must be rendered soluble in the digestive tract of an insect in order to be absorbed and exert a toxic action. Although the solubility of arsenicals is affected by the hydrogen-ion concentration, it is idle to solubilize arsenicals by adjustment of their *p*H before ingestion, since it has been found that arsenite solutions of various *p*H's show identical oral toxicity to insects.[35]

The solubility of the relatively insoluble lead arsenate increases in alkali; that of the relatively soluble calcium and magnesium arsenates decreases in alkali to almost nothing. Thus basic calcium arsenate is not dissolved in the alkaline (*p*H 8–9) digestive tract of *Bombyx* larvae and is excreted unchanged, but it is an active poison against *Dixippus* which has an acid (*p*H

6.6) alimentary canal.[114] Lead arsenate, although containing one-third less arsenic, is as effective as calcium arsenate against *Carpocapsa* larvae, whose stomach *p*H is 8.5.[77]

Since arsenicals are salts of weak acids, the effect of strong acid radicals in the insect gut is to liberate the free arsenical acid.[56] The principal acid in the alimentary canal of insects is not hydrochloric acid, but phosphoric acid. Thus ingested lead arsenate is transformed into insoluble lead phosphate and soluble arsenic acid or arsenate. The relative toxicity of lead, calcium, and magnesium arsenates to nine species of phytophagous insects has been found to parallel the degree to which arsenic is made soluble on standing in phosphate buffer adjusted to the gut *p*H of the respective insects.[137]

There is evidence that when the solubilized arsenic is in the form of dissociated arsenical ions, instead of the undissociated acid, the toxicity is reduced, presumably owing to decreased absorption. It was found that sodium arsenite, Paris green, sodium fluosilicate, and sodium fluoride showed little toxicity to certain lepidopterous larvae whose gut *p*H's were between 9.2 and 9.7 and in which the arsenic would be expected to be in the form of dissociated salts. Conversely the toxicity of these compounds was considerably higher to the migratory locust, which has a stomach *p*H of 6.8 and in which the acid radical would be expected to be undissociated.[27]

Specific susceptibility to insecticides

The most important single factor determining the susceptibility of a particular insect species to an insecticide is the extent to which the poison is prevented from reaching its site of action in the vital organs and tissues. Many circumstances may contribute to this prevention by setting up a series of impediments or barriers.

The very habitat of the insect may set up the first barrier. The difficulty of controlling stem borers and seed weevils is a case in point, and in most cases disinfestation methods are replaced by stem, wood, or seed treatments to prevent infestation in the first place. On the other hand aquatic larvae in a pool not only are defenceless, but also can no more escape the dissolved

insecticide than insects exposed in a fumigation chamber can avoid the vapour diffusing under the same gas laws.

A mobile insect such as the cockroach is hard to control, for it will escape from the area treated. Honeybees, perhaps possessed of intelligence in addition to reflex response, will leave fields when they are dusted or sprayed. The stick insect spits out the poisons and backs away.[66] Very occasionally it happens that insects refuse to feed on poisoned food, and it is common with arsenicals that certain species will avoid eating enough for a toxic dose. Mosquito larvae are repelled by aromatic oils and will not rise to contact the toxic surface film.

Active insects that live an exposed life have their susceptibility to control by contact insecticides reduced by thorough cuticular sclerotization. The tracheae are vulnerable points in some species, especially those with well-ventilated respiratory systems such as locusts and flies. Other species such as the honeybee can respond by tight closure of the spiracles, but most highly organized active species are rendered susceptible by their cuticular sensilla or tarsal sense organs.

Insects that dwell in crevices of the vegetation are extremely hard to control with contact insecticides. The aphid *Myzus persicae*, which is susceptible to control by DDT when infesting open laminate leaves like peach or potato, can be controlled only by a fumigant such as BHC when inhabiting the foliage of spinach. Caterpillars feeding within sheaths, such as the corn earworm, or within leaf rolls, such as *Argyrotaenia citrana* and *A. velutinana*, survive DDT applications in appreciable numbers; it is of interest that DDD is superior for these species. Larvae of *Ephestia* are resistant to residual poisoning by DDT, partly owing to their spinning a platform of silk which prevents contact with the deposit of insecticide.

At the other extreme there are the resting stages, the pupa being especially resistant because it does not feed, its respiration is low, and it is protected against contact poisons. These protective shields are cocoons (Hymenoptera and Lepidoptera), advanced cuticular sclerotization (Diptera), and a thickly waxed epicuticle (Lepidoptera). In addition, the pupa lacks the skin sensilla that make the equally armoured adult stage susceptible to contact insecticides. The egg is another comparatively re-

sistant stage, although it is not protected to the same extent by sclerotization or wax.

The following paragraphs will attempt to cover individually the various factors which may decide relative susceptibility or relative resistance. In few cases will they be found to be truly endogenous or intrinsic to the tissues of the insect. However, this may be the explanation for differences in congeneric species, such as *Crioceris 12-punctata*, which requires 16 times the dosage of DDT that kills *C. asparagi;* or *Protoparce sexta*, which is comparatively resistant to DDT, whereas *P. quinquemaculata* is very easily controlled by this insecticide.[123] It is probable that the DDT-resistant strains of *Musca domestica* in California and Illinois owe their resistance to endogenous factors (see Chapter XI).

Character of the cuticle. The outer defences of the insect's body are provided by cuticular secretions, such as the armoured shields of certain coccids and the waxy hairs of mealy bugs and certain aphids. Many adult beetles are covered with a secretory layer (*Sekretschicht*) which reduces their wettability by contact sprays, and in some species sand grains may be incorporated in it to form a protective layer.[70] In certain Hemiptera such as *Rhodnius*, the epicuticular lipoid is covered by a thin layer of resistant cementing material.[5] Some insects, such as *Psylla* and the larvae of *Psilopa*, have hydrophilic cuticles which resist wetting by oils. The larval cuticles of *Mamestra*, *Polia*, and *Musca* have both hydrophilic and lipophilic properties.[93a]

Cuticular hairs and spines serve to protect the insect against sprays by preventing full wetting of the underlying cuticular surface. The dense hairs of arctiid and nymphalid larvae render them resistant to control with insecticidal dusts.[93] The larva of *Euproctis*, although its integument is thin, is protected by a dense covering of long hairs (Fig. 13), so that it is not one of the most susceptible species.[66] A progressive increase in cuticular hairiness between the species *Tribolium* < *Calandra* < *Rhizopertha* < *Ptinus* in the adult stage is paralleled by a progressive increase in their resistance to poisoning by DDT dusts.[20a]

The presence of a thick waxy epicuticle in subterranean phalaenid larvae (cutworms) renders them resistant to contact

poisoning by pyrethrins, rotenone, and DDT. The more solid the wax, i.e. the higher its melting point, the more refractory the cuticular surface is to wetting by contact sprays.[5] A fluid grease, such as covers the integument of blattids, not only is less hydrophobic than a hard wax,[93a] but also offers a ready means of transport for contact poisons to all parts of the body surface, especially the susceptible underbelly region.[63,127] It is possible that this effect is also produced by non-fluid epicuticular lipoids serving as channels for the surface diffusion of liposoluble insecticides.[61]

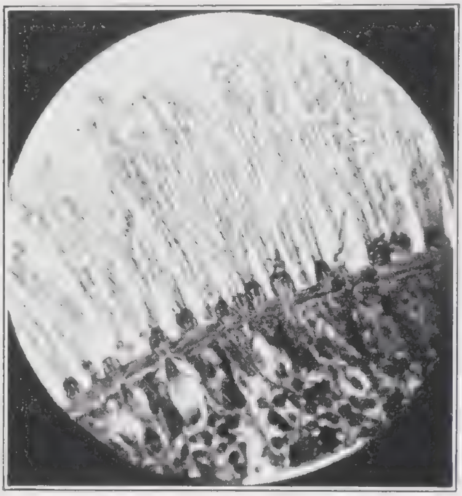


FIG. 13. Transverse section of cuticle of *Euproctis chrysorrhoea,* fourth-stage larva, showing the hairy tubercles. (After Klinger; courtesy of Deutscher Entomologischer Institut, Biologischer Zentralanstalt.)

The thickness of the exocuticle and the degree of sclerotization also afford a measure of protection against the entry of contact insecticides, as in the larvae of *Phyllophaga* and *Agriotes*, adults of bees and wasps, and nymphs and adults of roaches and locusts. The majority of adult beetles are extremely well protected in this respect. Not only is exocuticular tanning highly developed, but also the cuticle has been laid down as a meshwork of hardened rods or *balken* embedded in a continuous matrix.[48] The heavily sclerotized elytra with their air-filled columnae afford additional protection from contact poisons. The stick insect *Dixippus* (*Carausius*) owes its extreme resistance to a cuticular structure composed of *Balken* and an unusually hard exocuticle.[66]

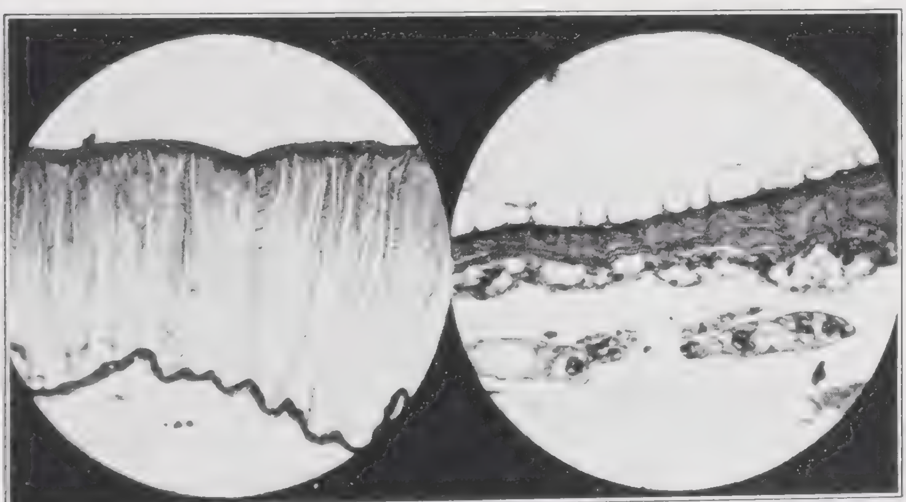
The gross thickness of the cuticle is an important factor in determining resistance to contact insecticides. The decreasing susceptibility of larvae and nymphs as they proceed into the older stages may be mainly ascribed to this factor. In Table 8 the decreased mortality of fifth-stage caterpillars as compared with the preceding stage, when exposed to pyrethrin sprays of

similar concentration, is seen to be associated with a thickening of the cuticle that is as much as fivefold in *Lymantria*.[66]

TABLE 8. Cuticle Thickness and Susceptibility of Caterpillars to Contact Sprays of Pyrethrins[66]

Species	Stage IV		Stage V	
	Cuticle Thickness, μ	Per Cent Mortality	Cuticle Thickness, μ	Per Cent Mortality
Bombyx mori	24	100	95	90
Dendrolimus pini	125	100	155	35
Lymantria monacha	27	35	145	0
Stilpnotia salicis	33	20	41	0

Similarly it has been discovered that well-fed *Rhodnius* nymphs, which consequently develop a thick cuticle, resist paralysis by pyrethrins for a period 3 times longer than do starved nymphs with a thin cuticle.[159] The resistance of *Carpocapsa* larvae to pyrethrins is associated with a thick dense cuticle with relatively few pore canals (Fig. 14). The larva of the rhinoceros beetle *Oryctes*, which has an extraordinarily thick cuticle with dense lamellae, and which lacks an epicuticle, is highly resistant to contact poisons.[66]



A B

Fig. 14. Transverse section of cuticles of naked larvae. A. *Mamestra brassicae*. B. *Carpocapsa pomonella*. (After Klinger; courtesy of Deutscher Entomologischer Institut, Biologischer Zentralanstalt.)

However, the comparative thicknesses of cuticle do not furnish a reliable index of relative susceptibilities of different species. In aquatic larvae of Diptera, the highly impermeable cuticle of *Corethra plumicornis* is only 2 μ in thickness, whereas the very permeable cuticle of *Chironomus plumosus* is as much as 7 μ thick.[3]

Cuticular sensilla and epidermal sense cells. Many species of bees, wasps, and flies are susceptible to contact insecticides when in the adult stage, in spite of possessing thick hardened cuticles. This is due to the abundance of cuticular sense organs, which serve as points of exposure outside the main defences of the insect. Conversely many larvae, and particularly maggots, are comparatively resistant to contact poisoning despite their unsclerotized cuticles, because of the scarcity or lack of skin sense organs.[66]

It has been noted above that the membranes at the base of the hair sensilla are a preferred point of entry for oil solutions of insecticides, whether they are thin areolae, as in *Tenebrio* larvae,[166] or set in thicker plaques, as in *Rhodnius* nymphs, and allow ready access to the sensory cells and nerve endings. The hair sensilla of the smooth-skinned *Smerinthus* larva and the spiny *Vanessa* caterpillar render them alike susceptible to pyrethrin sprays. The great susceptibility of *Bombyx* larvae is largely due to the abundance of microtrichia on its cuticle.[66]

The campaniform sensilla on the trochanters of roaches have been considered to offer a particular site of entry for DDT, leading directly to the sensory nerves, although this region of the body proved not to be a vulnerable spot for applications of pyrethrins.[124] The fact that the sensilla are located high up on the legs may have some bearing on the indifference of the cockroach to residual deposits of DDT.

On the other hand the flies *Musca* and *Glossina*, and to a lesser extent the bee *Apis*, are highly susceptible to residual deposits of DDT, which may be related to the fact that they bear tarsal chemoreceptors with cuticular sensilla on the plantar surface of their tarsi. *Epilachna* and *Oncopeltus*, which lack tarsal chemoreceptors, are comparatively immune to deposits of DDT over surfaces on which they walk.[59, 12] Where *Apis* is paralysed by

DDT dust in 20 min, the paralysis of *Stagmomantis* and *Cimex* involves 60 and 350 min, respectively.[126]

When a number of species were compared for their susceptibility to residual contact poisoning from DDT deposits, *Musca* and *Aedes* proved outstanding in susceptibility, the threshold lethal deposits being 1000 times lower than for the next most susceptible species, *Pediculus*. The body louse was followed in susceptibility by *Cimex*, *Blatta*, *Tribolium*, and *Sitophilus*; and finally *Rhodnius*, *Ornithodorus*, and *Tenebrio* larvae proved to be the most resistant.[12a]

The pulvillus of the housefly also offers channels of entry by way of hollow tenent hairs to an interior gland cell connecting directly with nerve bundles. Contact of the pulvilli of *Glossina* with pyrethrins causes almost immediate paralysis; they have to be in contact with DDT films for only 2 sec in order that death may ensue.[101] *Oncopeltus* also has well-developed pulvilli but normally walks on its claws, and bears down on the pulvilli only when the surface is smooth.[125]

Dermal glands and pore canals. The observation that the ducts of the dermal glands serve as points of entry for contact oils in *Rhodnius* adults suggests that these may provide vulnerable points in adult insects otherwise well protected by cuticular secretions. The more rapid penetration of pyrethrins in *Rhodnius*, where the pore canals have been straightened and shortened by cuticular stretching, indicates their importance as channels of penetration.[159] It has been found that the susceptibility to contact poisoning of larvae with many pore canals, such as *Bombyx*, *Smerinthus*, or *Dendrolimus*, is much greater than that of a caterpillar with very few pore canals, such as *Carpocapsa*.[96] Yet mosquito larvae are highly susceptible to contact poisoning despite an entire absence of pore canals in the cuticles.

The ensemble of integument characteristics. The researches of Klinger on many species of lepidopterous larvae have elucidated the relation of cuticular structure to their susceptibility to contact insecticides. On the one hand resistance is conferred by cuticular thickness, the presence of hairs and spines, cuticular sclerotization, and a repellent epicuticle. On the other hand susceptibility is increased by the presence of hair sensilla or microtrichia, an abundance of pore canals, and a receptive

epicuticle. These findings are summarized in Table 9, where the species are listed in order of their susceptibility for comparison with their cuticular characteristics.

TABLE 9. INTEGUMENTAL CHARACTERISTICS OF CATERPILLARS AND THEIR SUSCEPTIBILITY TO CONTACT INSECTICIDES [66]

Species	Cuticle	Sensilla	Pore Canals	Epicuticle	Hairs	Per Cent Mortality			
						Pyrethrins		Rotenone	
						Spray	Dust	Spray	Dust
Bombyx mori					–	100	100	100	95
Vanessa io		Many	Many	Wettable	++	100	95	45	15
Smerinthus ocellata	Thin				–	100	80	5	0
Dendrolimus pini					+	100	90	15	5
Euproctis chrysorrhoea					+++	100	50	10	0
Euxoa segetum		Few		Repellent	–	20	5	0	0
Mamestra brassicae	Thick				–	0	5	0	0
Carpocapsa pomonella			Few		–	0	0	0	0

Digestive system and susceptibility to stomach poisons. The minimum lethal doses of sodium arsenite necessary for stomach poisoning of three species of insects were found to be as follows: *Euxoa segetum*, 0.14 mg/gm; *Pieris brassicae*, 0.04 mg/gm; and *Locusta migratoria*, 0.03 mg/gm, expressed as elemental arsenic.[149] The greater resistance of *Euxoa* as compared to the other species may be traced to four characteristics of its digestive system. The ingestion of arsenite induces regurgitation as a result of ventricular spasms, an effect not realized in *Pieris*. It promotes diarrhoea in *Euxoa* and *Pieris* but has the opposite effect on *Locusta*. The rate of intestinal absorption of arsenite is less in *Euxoa* than in the other two species. The rate of excretion of arsenic by the Malpighian tubules is faster in *Euxoa* than in *Pieris* or *Locusta*.

The minimum lethal doses of rotenone by mouth show even greater interspecific variation: *Bombyx mori*, 3 mg/gm; *Vanessa cardui*, 30 mg/gm; *Heliothis obsoleta*, 500 mg/gm.[168] Rotenone is entirely non-toxic to *Prodenia* larvae, since it is not absorbed by the intestine. Whether resistance depends primarily on the

lack of absorption, or is attributable to a paralysis of the mouthparts, is a matter for further study. It is probable that resistance to stomach poisoning by pyrethrins, where it occurs, is due to intestinal hydrolysis of the poison.[169]

Endogenous susceptibility. Certain factors deciding the relative susceptibility of various species to insecticides may reside within the organization of the tissues. For example, tissue homogenates of certain DDT-resistant strains of the housefly are able to dehydrohalogenate DDT more rapidly than normal. Increasing use of body-cavity injection methods of toxicity assessment will serve to elucidate this problem. At present the factors that fall in this class are those that cannot be related to penetration. For instance, larvae of *Lymantria monacha* are much more resistant than those of *L. dispar* to pyrethrin poisoning, not because of a more impenetrable cuticle, but because their nerves and ganglia are relatively immune from histological damage. Perhaps similar considerations will account for *Stilpnotia* larvae being more resistant than *Dendrolimus* larvae to this poison in spite of having thinner cuticle and a greater abundance of pore canals and microtrichia.[66]

The hydrogen-ion concentration of the haemolymph may possibly be a cause of endogenous variation in susceptibility. Studies of a few forest insects suggested that resistance to certain contact poisons was associated with greater alkalinity, i.e. a higher *p*H of the haemolymph. From the few species investigated, there was a faint suggestion that the hairy caterpillars had a more alkaline haemolymph, and that the blood of the naked larvae was more acid.[40]

More exact studies on ten species of insects gave the following ranges in *p*H associated with four classes of susceptibility: very susceptible, 6.8–8.0; moderately susceptible, 6.4–7.2; moderately resistant, 5.8–6.9; very resistant, 6.6. These results suggested that resistance to pyrethrin and rotenone poisoning showed a tendency to be associated with greater acidity, i.e. lower *p*H of the body fluids. However, the most resistant species, *Dixippus morosus*, with a blood *p*H of 6.6, proved to be just as susceptible as the other species when the pyrethrins were injected directly into the haemolymph; thus its resistance appears to be due to

the lack of cuticular penetration and not to an endogenous quality such as blood acidity.[66]

Developmental age and susceptibility to contact insecticides. It is generally observed that as larvae increase in age and pass into the later stadia, they become more resistant to contact insecticides. In some cases almost complete immunity is reached at the prepupal stage. The figures summarized in Table 10 illustrate this point. It is probable that in most cases

TABLE 10. STAGE OF DEVELOPMENT AND SUSCEPTIBILITY TO PYRETHRIN SPRAYS[66]

Larvae of the satin moth (*Stilpnotia salicis*)

Stage	Per Cent Kill	Period of Kill
I	100	12 hr
II	100	16 hr
III	100	3 days
IV	65	4 days
V	15	5 days
VI	5	5 days

the main factor is an increase in cuticle thickness, often associated with a thicker sclerotized exocuticle. The sudden increase of resistance of the silkworm larva on reaching the fifth instar is attributable not only to the factors mentioned, but also to a decrease in the number and size of pore canals and microtrichia. A larva is often unusually susceptible to contact poisoning immediately after moulting, when the cuticle is still thin and the pore canals are still filled with cytoplasmic processes, as has been observed with *Dendrolimus*.[66]

A correlation between the lipoid content of the cuticle and the susceptibility of *Loxostege* larvae to contact poisoning by pyrethrins has been noted. The cuticle of the susceptible third-stage larva was found to consist of 12% fat, whereas that of the practically resistant fifth-stage larva contained only 0.2% fat. There was no significant change in protein or chitin content between instars.[96]

Relative susceptibility to sprays and dusts. Methods of practical application favour the use of dusts for control of some species, and sprays for others. In most cases it is clear that

the choice is directed by considerations of ease of application, the crop to be protected, or the habits of the insect. The requirement dictated by the physiological characteristics of the insect may be checked by applying equivalent amounts of insecticide in dust form on the one hand and in oil spray on the other. The mortality resulting from application of pyrethrins and rotenone at a deposit rate of 0.38 $\mu g/cm^2$, either dissolved as a spray in Turkey-red oil or formulated as a dust with powdered talc,[145] is shown in Table 11. The results show that the oil solutions of

TABLE 11. RELATIVE SUSCEPTIBILITY TO SPRAYS AND DUSTS [145]

Per cent mortality from 0.38 $\mu g/cm^2$ deposits of the insecticide

Species	Spray		Dust	
	Rotenone	Pyrethrins	Rotenone	Pyrethrins
Bombyx mori	98	100	100	100
Agelastica alni	95	100	80	100
Vanessa polychloros	30	100	10	100
Euproctis chrysorrhoea	15	100	0	
Athalia spinarum	10	100	..	..
Dendrolimus pini	4	100	8	96
Vanessa io	0	100	0	90
Vanessa urticae	0	100		..
Smerinthus ocellata	0	100	0	..
Agrotis sp.	0	5	0	10
Lymantria monacha	0	0		.
Stilpnotia salicis	0	0	0	0
Carpocapsa pomonella	0	0	0	0
Oryctes nasicornis	0	0		..
Melolontha sp.	0	0	.	.
Myzus persicae	0	0		..

the insecticide are slightly more effective than the dust mixtures for most of the species where a comparison was possible. It should, however, be pointed out that talc is a non-abrasive dust. Similar results were obtained in a second study on several species of insects, in which the deposit densities were not stated.[66]

Thus the effects of the oil solvent in ensuring continuous coverage of the cuticle, aiding cuticular penetration, and promoting tracheal entry are reflected as practical advantages. How far abrasive dusts can increase cuticular entry to surpass that ob-

tained with oils requires investigation. It is clear, however, that as a general rule insects are more susceptible to oil sprays than to non-abrasive dusts.

Relative susceptibility to fumigants

Variation between species. The rice weevil (*Sitophilus oryzae*) is much more susceptible to chloropicrin fumigation than the granary weevil (*S. granarius*), the difference in susceptibility being much greater than that between species of different orders. Larvae of *Hyponomeuta* are much more susceptible than the related *Ephestia*. The male *Blatta* is more susceptible than the female. In each case the greater susceptibility to chloropicrin vapour was correlated with a greater ability to lose water when the insect was kept in a vacuum desiccator.[94]

TABLE 12. Relative Resistance to Narcotic and Toxic Fumigants[12]

Median lethal dose, mg/litre

Species	Narcotic Fumigants			Toxic Fumigants				
	Benzene	Trichloroethylene	Carbon Tetrachloride	Ethyl Acetate	Ammonia	Hydrogen Cyanide	Ethylene Oxide	Sulphur Dioxide
Sitophilus granarius	213	251	592	99	8.9	22	17	10
Sitophilus oryzae	183	219	473	36	7.3	24	12	31
Ephestia kuehniella	152	204	448	50	7.7	0.4	26	16
Tineola bisselliella	137	176	352	69	....	6.5	18	24
Tribolium castaneum	64	103	137	68	5.9	0.6	41	17
Cimex lectularius	62	67	113	25	12	0.14	26	6.7

When six species of household insects were tested for their relative susceptibility to six different narcotic fumigants (see Table 12, where 3 narcotics are listed), they were found to arrange themselves in roughly the same order of susceptibility no matter which fumigant was employed; moreover the differ-

ences between the species were not very great. But the order of their susceptibility was found to vary quite considerably to vapours of acetate esters, ammonia, sulphur dioxide, and ethylene oxide, and the species varied extremely widely in their susceptibility to hydrogen cyanide.[12] Whereas both species of *Sitophilus* were more resistant than *Tribolium* to ethylene oxide, *Tribolium* was more resistant than *Sitophilus* to hydrogen cyanide, in spite of having a considerably higher normal rate of respiration.[72]

The susceptibility to fumigants shows no correlation with the relative normal activity of the species. Rather, the rising order of susceptibility to hydrogen cyanide—*Blattella* < *Tribolium* < *Tenebrio* < *Lasioderma* < *Sitophilus*—was found to be correlated to the total amount of this compound which was "sorbed" before death.[15] It would appear that the difference in resistance between insects was correlated more with their ability to exclude foreign vapour when the occasion demanded it. This, coupled with the correlation of resistance with the ability to prevent water loss (see above) points to effective control of tracheal ventilation as the main factor in determining resistance of a species. It is probable that the degree of tracheal ventilation of an insect, and consequently its susceptibility to a particular fumigant, depend on whether it is stimulated or stupefied by the initial exposure to the vapour. Different compounds evoke different responses, and the response to any one compound differs from species to species. Small doses of carbon disulphide are typically stimulant, so that an initial exposure of *Sitophilus* to a sublethal concentration increases its susceptibility to carbon disulphide fumigation commenced a few minutes later.[131] Hydrogen cyanide is typically stupefying or narcotic, so that initial exposure of *Aonidiella* to a sublethal concentration decreases its susceptibility to hydrogen cyanide fumigation commenced an hour later.[73] It is considered that this "protective stupefaction" is due to the cessation of mechanical ventilation of the tracheae; it is shown also by *Sitophilus*, but not by *Tribolium* or *Hippodamia*. Investigations made with the aim of discovering stimulant auxiliary gases for cyanide fumigation showed that whereas chloropicrin was stimulating to the lady-beetle *Hippodamia*, it was stupefying to the scale insect *Saissetia*. Al-

though benzyl chloride was stimulating to both species, benzaldehyde and acetophenone were stimulating only to *Hippodamia*.[20] Whereas *Coccus* and *Saissetia* were also stupefied by HCN, grasshoppers proved to be stimulated into hyperactivity. Nicotine in low dosages also was found to render the grasshopper *Chortophaga* hyperactive,[80] but it depressed the mechanical ventilation of the roach *Nyctobora* at all concentrations.[55]

Carbon dioxide in low concentration causes the spiracles to open,[157] although in high concentration it decreases ventilation movements because of its narcotic effect. Addition of small amounts of this gas to carbon disulphide, chloropicrin, ethylene dichloride, or ethylene oxide was found to enhance the toxicity of these compounds to *Tribolium* or *Sitophilus*.[18] However, it proved to decrease the toxicity of hydrogen cyanide to *Hippodamia* or *Saissetia*, although increasing it to the resistant strain of *Aonidiella*.[20]

The application of a moderately high vacuum also causes the spiracles to open because of the lack of oxygen.[157] The effectiveness of hydrogen cyanide on *Tribolium* rises steadily as the air pressure drops to 2 mm Hg, as also does the capacity of the flour beetle to "sorb" cyanide. With *Sitophilus oryzae*, however, both toxicity and sorption are at a maximum at 60 mm pressure, when the insects are still active; at lower pressures the weevils become quiescent and the uptake of cyanide is progressively inhibited. If the vacuum is replaced with nitrogen the enhancement of the toxicity of hydrogen cyanide to *Tribolium* is no longer maintained.[82]

A race of *Aonidiella aurantii* has appeared in California which is considerably more resistant to hydrogen cyanide fumigation than the normal stock. Although for the most part there is no detectable difference in the chemical composition of the two strains, the resistant strain was found to contain only one-tenth of the normal content of copper.[13] This finding is consistent with the known fact that administration of copper increases the susceptibility of citrus trees to damage by cyanide vapour. The difference between the two strains has been more closely associated with spiracular movement.[15] In both races the spiracles pulsate from the fully open to the partly closed position at the

rate of 60 pulsations per minute. Exposure of the normal stock induces spiracular closure for 1 min only, whereas the resistant stock will respond by keeping the spiracles closed for a period of 30 min. However, the difference in resistance between the races is apparent even in 2-min exposures to hydrogen cyanide, when the spiracles in both cases open and close at the same rate,[105] and tracheal ventilation is presumably equal. The "protective stupefaction" effect of hydrogen cyanide on the resistant race of *Aonidiella* is negligible.[73]

Variation between developmental stages. In holometabolous insects it is generally found that the larva is the most susceptible stage to the toxic effect of fumigants, its median lethal dose being less than for other stages (Table 13). This occurs in spite of the fact that in most insects, such as *Tribolium*, the larval respiratory rate is lower than in the adult[72] (Fig. 15). The pupa with its low respiratory rate is the least susceptible stage, except where its resistance is exceeded by the egg. In some species and for some fumigants the egg is the most susceptible stage, in others the most resistant. In the tests of

TABLE 13. Relative Susceptibility of Developmental Stages to Fumigants

1, most susceptible; 4, most resistant. Y., young; O., old.

Insect	Fumigant	Order of Susceptibility			
		1	2	3	4
Tribolium[41]	Hydrogen cyanide	Egg	Larva	Adult	Pupa
Lyctus[11]	Hydrogen cyanide	Larva	Adult	Pupa	....
Tribolium[72,134]	Carbon disulphide	Larva	Adult	Pupa	Egg
Ephestia[11]	Carbon disulphide	Adult	Larva	Pupa	....
Tribolium[72]	Chloropicrin	Larva	Adult	Pupa	Egg
Tribolium[72]	Ethylene oxide	Egg	Larva	Adult	Pupa
Cimex[11]	Sulphur dioxide	Y. nymph	Adult	O. nymph	Egg
Cimex[11]	Hydrogen cyanide	Egg	Y. nymph	Adult	O. nymph

fumigants on *Cimex*, the egg was also the most susceptible stage to ethylene oxide and *o*-dichlorobenzene, and the most resistant stage to trichloroethylene.[11] In tests performed on *Tribolium*,

the egg was more susceptible than the adult to methyl bromide and mercury vapour.[134] Under conditions of high relative humidity, the pupa of *Tribolium* was more resistant to carbon disulphide than the egg.[72] There is evidence that adult *Tribolium*, especially virgin females, emit a vapour which adsorbs and inactivates hydrogen cyanide.[41]

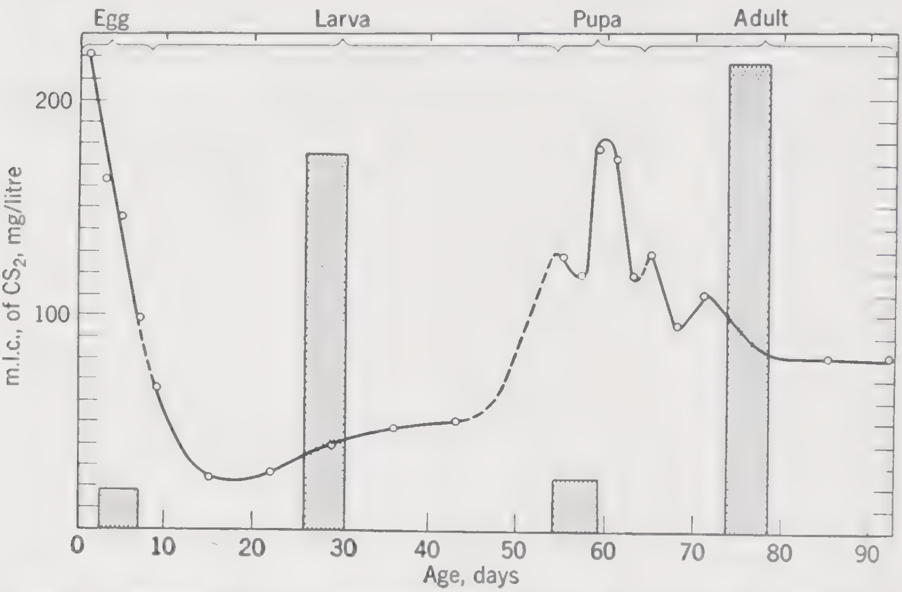


Fig. 15. Median lethal concentrations of carbon disulphide for *Tribolium* at various stages and ages. (From Sun). Histograms are added to represent the metabolic rate of the four developmental stages, using the same ordinate as milligrams CO_2 per gram of body weight per day. (From Lindgren)

The susceptibility of the pupa varies with its stage of development. The early pupal period, where histolysis is taking place, and the late period, where histogenesis is predominant, show a much higher respiratory rate than the intermediate part of pupal life.[157] It is in this middle period that the pupa is more resistant to fumigants, as evidenced by the median lethal concentration figures for *Tribolium* with hydrogen cyanide,[41] carbon disulphide,[134] ethylene oxide, and chloropicrin[72] (Fig. 16). It is also in the middle of pupal life that the capacity of *Musca* pupae to sorb hydrogen cyanide reaches a minimum.[74]

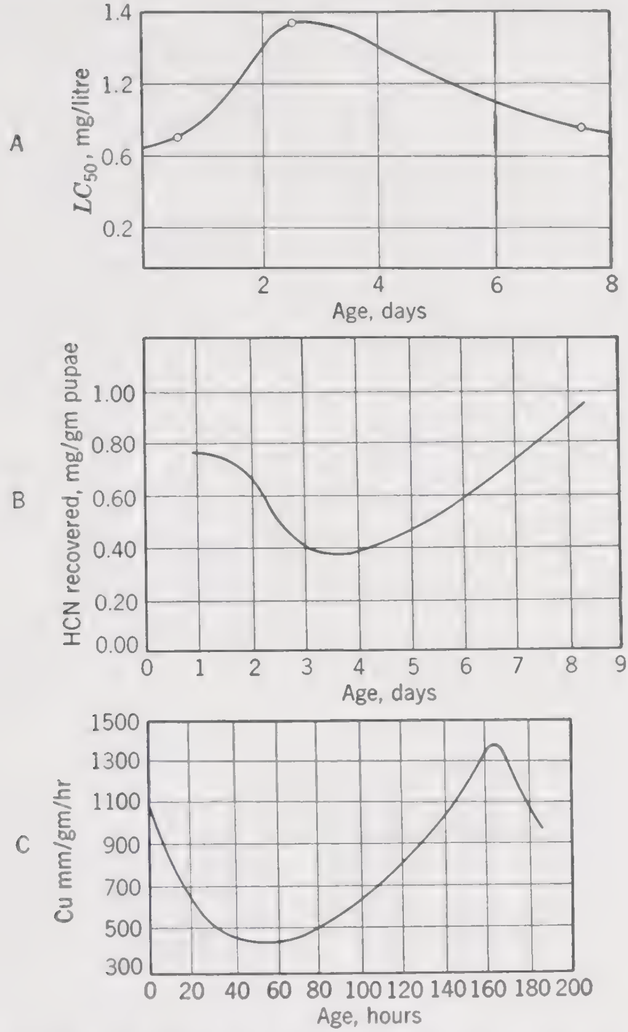


Fig. 16. Relation of toxicity of HCN to sorptive properties and respiratory rate in pupae. A. Toxicity to male *Tribolium* pupae. (From Gough). B. Sorption, as indicated by recoveries of gas, in *Musca* pupae. (From Lindgren and Sinclair). C. Oxygen consumption in *Galleria* pupae. (From Wigglesworth)

The effect of temperature upon mortality

Consideration of this topic is clarified by bearing in mind that two factors are involved in the toxic action of an insecticide. The first factor represents the speed and degree to which the poison is taken up by the insect and acts upon its tissues; and

the second involves the speed and degree to which the poison is eliminated by excretion, breakdown, or detoxification. With decisive doses of quick-acting poisons, it may therefore be expected that mortality is quicker and greater at a high temperature than at a low temperature of application. With marginal doses of slow-acting poisons the expectation is that recovery will be less at the low temperature than at the high, and that the mortality will be greater although it develops at a slower rate. The temperature of application decides the rate of uptake or the immediate toxicity, and the post-treatment temperature governs the rate of recovery.

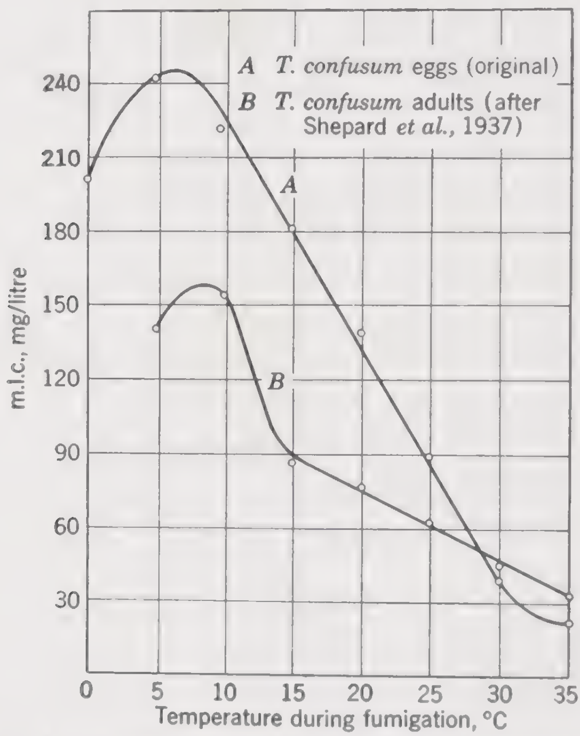


FIG. 17. Effect of temperature upon median lethal concentration of carbon disulphide for eggs and adults of *Tribolium*. (From Sun)

Temperature of application. At the higher temperature, at least in the working range of 10–30° C, most insects are in a more active state, more material is metabolized, and the reactivity of poisons in the biochemistry of the body is greater. The increase in respiration by diffusion or by respiratory movement will allow

a faster entry of poisons into the tracheal system. Cuticular penetration of rotenone in *Melophagus*, for example, was found to proceed faster at 30° than at 20° C.[152] And so it is found that as far as the temperature of application is concerned, mortality is greater at high temperatures than at low.

For equal doses of pyrethrin spray, 73% of *Eutettix* leaf hoppers were found to be killed at 100° F as against 53% at an application temperature of 60° F.[46] Injections of pyrethrins are twice as effective on *Galleria* larvae at 30° as at 20° C.[7] The toxicity to *Ahasverus* of immersion in derris extract at 25° C is 5 times that at 10° C.[19] The susceptibility of *Lymantria monacha* larvae to the qnick-acting contact poison DNOC rises with temperature.[55]

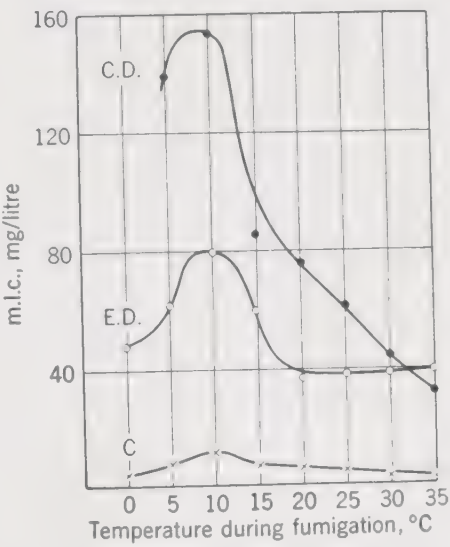


FIG. 18. Effect of temperature upon median lethal concentrations of chloropicrin, ethylene dichloride, and carbon disulphide for *Tribolium* adults. (From Shepard, Lindgren, and Thomas)

Houseflies exposed at 95° F to residual deposits of DDT for 40 min showed complete mortality, while exposure at 65° F for the same period (and with the same post-treatment temperatures) allowed a proportion to survive.[75] However, when houseflies were continuously exposed to residual deposits, greater mortality was obtained at 70° F than at 90° F with DDT, DDD, and methoxychlor, while the reverse was the case with toxaphene, chlordane, aldrin, dieldrin, and parathion.[54a]

The efficacy of fumigants, such as carbon disulphide or chloropicrin, increases as the temperature of fumigation rises from 10° to 35° C, for both eggs[131] and adults[129] of *Tribolium confusum*; below 10° C it increases also (Fig. 17). The same picture is shown by ethylene dichloride and chloropicrin (Fig. 18). This increase in susceptibility occurs despite a decrease in sorption of the fumigant at 30° C. One-third less hydrogen cyanide is sorbed

by *Sitophilus oryzae* at 30° C than at 20° C.[15] The temperature coefficient of toxic action was found to vary between 3.5 and 1.1, dependent on the species, developmental stage, and fumigant, in the range 20–30° C; the Q_{10} values were most commonly between 2.0 and 2.5.[11] Even the low-vapour-pressure fumigants, such as parathion, show an extremely pronounced increase in toxicity with temperature when applied to tetranychid mites.[123]

Post-treatment temperature. In the case of marginal doses of insecticides, or of working doses of slow poisons, the process of elimination of the poison from the body may become the critical factor in deciding survival or death. Since the processes of recovery are retarded at low temperatures, it may be expected that as far as the post-treatment temperature is concerned, mortality will be greater at low temperatures than at higher or more optimal temperatures. With the same stock of *Eutettix* as mentioned above, for an equal dose of pyrethrin spray applied at the same temperature of application, the mortality at a post-treatment temperature of 60° F was found to be 81–88% as against 29–33% at 100° F.[46] After being exposed to pyrethrin and *Lethane 384* sprays, houseflies showed a smaller percentage of recovery when kept at 20° C than at 38° C.[31] *Plutella* larvae that had been sprayed with 0.0125% suspensions of DDT showed only 9% mortality when subsequently held at 90° F as contrasted with 78% mortality when held at 70° F.[30] The stock of *Ahasverus* mentioned above showed greater mortality at a pre- and post-treatment temperature of 20° C than at 25° C.[19] Of the houseflies that had picked up residual films of DDT at 65° F, mortality was greater in those subsequently kept at 70° F than in those kept at 100° F.[75] Adults of the braconid parasite *Macrocentrus* showed higher and faster mortality when exposed to DDT deposits and kept at a temperature below 70° F than when the temperature exceeded 80° F.[98]

When either pyrethrins or rotenone is applied to bees by contact or *per os*, the mortality is greater if they are kept at 20° C than at 34.5° C, the susceptibility to pyrethrins being 10 times greater at the lower temperature. In the case of rotenone it was observed that although the eventual mortality was greater at the lower temperature, the action was faster at the higher temperature, so that for the first 3 days the mortality was greater than

that under the cooler conditions.[8] Similarly, although *Lymantria* larvae recover at 30° C from a marginal dose that would prove fatal at 20° C, with lethal doses they die more quickly at the higher temperature. At lower temperatures the mortality is higher but the larvae take a longer time to die.[66] Again when the rose chafer *Macrodactylus* has been sprayed with pyrethrins, subsequent exposure to a higher temperature (42° C) decides within a matter of seconds whether the outcome is to be death or survival, whereas at more normal temperatures the insect remains in a moribund condition.[47]

The toxicity of several contact insecticides to *Tribolium* has been compared for a post-treatment temperature of 60° F as against one of 80° F. With the exception of nicotine, all the insecticides were more toxic at the lower holding temperature. Pyrethrins were 4–7 times as toxic, DDT 2½ times, and lauryl thiocyanate and DNOC 1½ times as toxic at 60° as at 80° F. The temperature obtaining before treatment had on these ratios about half the effect of the post-treatment temperature.[100] Nicotine,* however, especially when residual vapour was present, was no more toxic at the lower temperature against *Tribolium*, and less toxic than at the higher temperature against *Apis*.[8] In similar experiments with *Blattella*, although DDT, lindane, and pyrethrins were more toxic at the lower holding temperature, aldrin and dieldrin were more toxic at the higher temperature.[12a]

Similar results are obtained with fumigants, where the mortality obtained at a postfumigation temperature of 20° may be less than half that at 5° C (Fig. 19). It is evident that a rise in temperature increases the rate of desorption of the fumigant from the cuticle and tracheae of the insect.[134] It also hastens the elimination of vapour from the tracheae because of an increase in the rate of diffusion at the higher temperature. These effects are additive to the usual increase in excretion and detoxification under warmer conditions.

The same general picture is evident in the case of inorganic stomach poisons. For calcium arsenate, acid lead arsenate, or

* Injected nicotine was more toxic at the higher temperatures to *Oncopeltus* nymphs, but more toxic at the lower temperatures to *Oncopeltus* adults (N. Woodruff. 1950. *J. Econ. Ent.*, **43**:663–669).

basic copper arsenate administered to larvae of *Prodenia* or *Anticarsia*, the toxicity at a holding temperature of 60° F was found to be approximately twice that at 80° F. Here again the mortality at the lower temperature takes a longer time to develop, as if the larvae had greater difficulty in freeing themselves of the poison.[33]

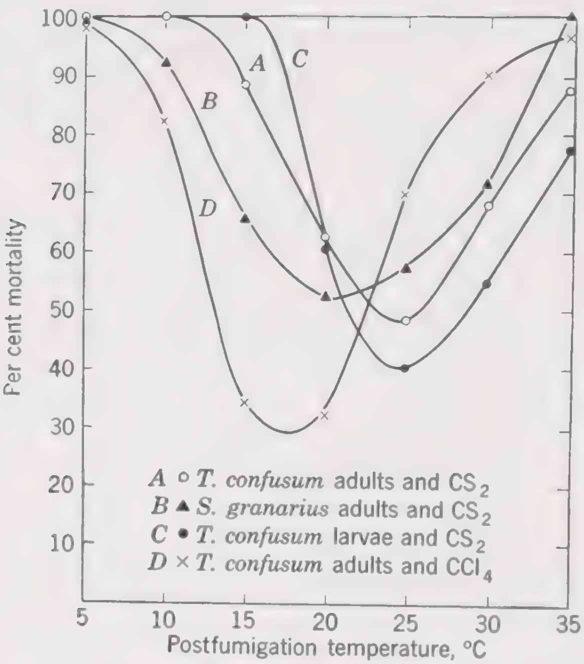


FIG. 19. Effect of postfumigation temperature upon the mortality of *Tribolium* and *Sitophilus* to carbon disulphide and carbon tetrachloride. (From Sun)

Although the mortality decreases as the post-treatment temperature is raised from 10° to 30° C, at higher temperatures it may start to increase as conditions of heat unfavourable to the insect are encountered. For instance with *Eutettix* the mortality after an application of pyrethrins increases slightly when the post-treatment temperature is raised from 90° to 100° F.[16] And with *Tribolium* and *Sitophilus* exposed to carbon disulphide, the mortalities increase as the postfumigation temperature is raised above 25° C.[134] From observations on the percentage recovery from pyrethrin poisoning shown by several insect species at various post-treatment temperatures, it has been concluded that the

optimum temperature for recovery coincides with the optimum developmental temperature for that particular species (Fig. 20). Moreover resistance was found to increase as the relative humidity approaches 100%.[40]

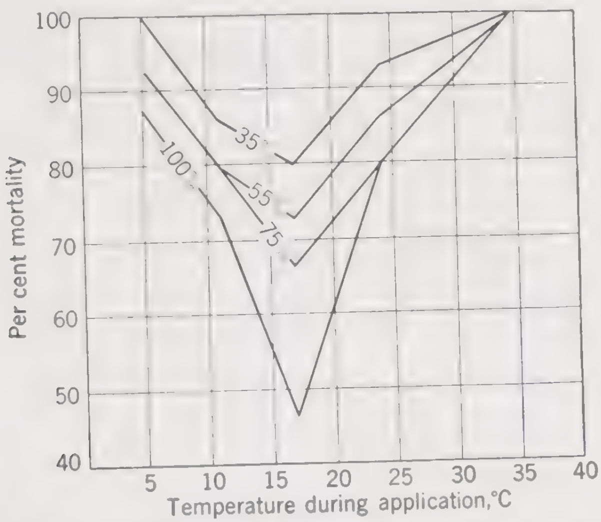


Fig. 20. Effect of temperature and relative humidity upon the mortality of *Dendrolimus* larvae to pyrethrum dusts. 35, 55, 75, and 100% relative humidity tested. (From Gosswald)

It may be concluded that best results will be obtained with insecticides when the application is made under warm conditions, followed by a period of cooler temperature. If only a single temperature level is available for both application and post-treatment holding, the cooler temperature is preferable, because of the more decisive effect of the post-treatment conditions.[16] There is evidence that it is best to avoid conditions of high humidity.

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CHAPTER IV

The Pharmacology of Poisons for Insects

Insect toxicology

In general, the chemicals available for the poisoning of insects are those which are already known to be toxic to higher animals and man. Some of the more obvious examples are the salts of mercury and copper, the arsenicals, cyanides, nicotine, and the organic phosphates. It is not surprising that this is so, since similar mechanisms for cellular metabolism apply throughout the animal kingdam.[1964] Thus at first sight it would appear a difficult task to obtain insecticidal compounds that are not also highly toxic to the animals and plants which they are intended to protect.

Insects present a more difficult problem to the poisoner in that they exhibit a less complicated array of organs and tissues than the mammal. They are more resistant because they have less to go wrong. They lack the lungs, liver, and cardiovascular system which provide the mammal with additional hostages to

fortune. The insect has only one type of nerve biochemistry, whereas the mammal evidently has three. Moreover, insects are free of the necessity of maintaining a delicate balance of metabolites in the blood and of depending on the pigment cells of the blood to supply oxygen to the tissues. They show a high degree of resistance to anoxia and can recover from deep oxygen debt. They are able to recover from appreciably high narcotic doses of hydrogen cyanide. The median lethal dosage levels of our present most powerful insecticides (see Table 1) still considerably exceed those of the most potent toxins for mammals, which are less than 10 μg/kg.[31]

TABLE 1. Median Lethal Doses of Insecticides Applied by Contact [11]

Doses in mg/kg; these are maximal figures.

Insecticide	*Musca domestica*		*Aedes aegypti*	
DDT	7	10	5	7
Lindane	2	3	2	3
Pyrethrins	35	40	0.5	0.75

However, circumstances may combine to make the application of certain chemicals considerably more toxic to the insect than to the organism to be protected. The extreme voraciousness of phytophagous larvae renders them susceptible to arsenicals applied to their food in a concentration insufficient to endanger the plant or the higher animal that competes for it. The fact that the insect has respiratory openings along the length of its body makes it vulnerable to applications of mineral oils which are practically non-toxic to mammals. Pyrethrins appear to be specifically insecticidal because the insect cannot detoxify them as rapidly as warm-blooded animals can. And certain substances which are not particularly dangerous poisons, such as DDT and DNOC, may be found to be effective insecticides as a consequence of their attraction to the insect cuticle.

The small size of insects and the comparative thinness of their cuticle have left their nervous system insufficiently protected. The extension of the nervous system into the cuticular sense organs of the legs is an especially vulnerable feature. The most recently developed insecticides are nerve poisons. Since the central nervous system of the insect is cholinergic, it is particu-

larly susceptible to that class of poisons described as anticholinesterases. An obvious advantage of nerve poisons as insecticides is that they are without toxicity to plants, which offer no site of action.

Classification of insecticides

The customary classification of insect poisons into three groups—stomach insecticides, contact insecticides, and fumigants—is based upon their mode of entry into the insect. This classification, with its limitations, has been discussed in the previous chapter.

A more natural basis for classification of insecticides is their mode of action, and it may be derived from the pharmacology already established for mammals. However, certain groups of mammalian poisons are not represented in the insect pharmacology. The cardiovascular drugs, such as digitalis and histamine, have no effect on the insect. Certain autonomic drugs, such as adrenalin and curare,* are without appreciable effect on the intact insect, whereas others, such as eserine and nicotine, are highly active.[39, 53, 111] Strychnine, which stimulates the central nervous system of mammals and is thereby highly toxic to them, is neither stimulant nor toxic to insects.[38] Poisons of the mammalian blood cells, such as lysolecithin, have no insecticidal toxicity.[165]

On the other hand, practical insect control may avail itself of a greater variety of weapons than the type of mammalian control known as chemical warfare. In the latter case, only very powerful poisons, such as dichlorodiethyl sulphide and lewisite, can be used as contact homicides. The weapons available are generally limited to compounds which can enter the lungs as a vapour, for example the true toxic gases, such as hydrogen cyanide, and the lung irritants, such as phosgene. For the control of insects, the ease with which they may be poisoned by contact allows even nerve poisons to be applied in sprays or dusts. Moreover, since in most cases insects lack the means of detecting poisons by taste or smell, they may be controlled by large-scale contamination of their food by stomach insecticides.

* Adrenalin and curare are capable of slowing and arresting the insect heart isolated from nervous connections.[40]

1. Physical poisons. These materials characteristically exert a physical rather than a biochemical effect. When they are applied for insect control, they are logically reinforced by insecticidal compounds.

(*a*) Heavy mineral oils and tar oils. Highly refined mineral oils may exert a purely asphyxiant effect, killing scale insects slowly by exclusion of air. Dormant oils smother insect eggs for a sufficient length of time to asphyxiate, but their action is hastened by the toxic impurities nearly always present in such materials.

(*b*) Inert dusts. These effect a loss of body moisture from the insect by two types of action. Abrasive dusts, e.g. aluminum oxide, cause water loss by lacerating the epicuticle. Water-adsorbent materials, e.g. charcoal, remove water as a consequence of their hygroscopic properties. Certain dusts may combine both characteristics.

2. Protoplasmic poisons. The action of these poisons appears to be associated primarily with the precipitation of protein.

(*a*) Heavy metals, e.g. compounds with Hg and Cu.

(*b*) Alkaloidal reagents, e.g. nitrophenols and nitrocresols.

(*c*) Acids. Examples are fatty acids, which are contact insecticides, and mineral acids, which do not normally penetrate the cuticle. Mineral acids may be produced secondarily within the tissues from the halogenated fumigants or from SO_2.

(*d*) Formaldehyde and ethylene oxide.

(*e*) Fluorides, fluosilicate, and fluoaluminates, borates, arsenates, and arsenites. These inorganic stomach poisons appear primarily to destroy the cellular protoplasm of mid-gut epithelium.

3. Respiratory poisons. These include HCN, H_2S, and CO, which are respiratory poisons not only in the sense of being fumigants, but also in that they block cellular respiration. They combine with cytochrome oxidase and other oxidases containing Fe, and thus inhibit their catalytic action.

4. Nerve poisons. The action of these poisons is associated primarily with their solubility in the tissue lipoids.

(*a*) Chlorinated hydrocarbons: CCl_4, ethylene dichloride, PDB, DDT, lindane, etc.

(*b*) Aromatic and olefinic hydrocarbons: naphthalene, kerosene, gasoline, etc.

(*c*) Botanical insecticides: pyrethrins, nicotine, sabadilla, etc.

(*d*) Organic phosphates (anticholinesterases): HETP, TEPP, parathion, etc.

(*e*) Miscellaneous: CS_2, valone, piperine, aniline, etc.

5. Poisons of a more general nature.

(*a*) Chlordane, toxaphene, aldrin, dieldrin; these chlorinated terpenes do not induce neurotoxic symptoms until a latent period has passed.

(*b*) The *Lethanes, Thanite;* these organic thiocyanates have an immediate depressant effect.

(*c*) Rotenone, ryania, phenothiazine; these are muscular depressants, of which the first two may induce slight neurotoxic symptoms.

Specific action of insect poisons

Attempts to trace the effect of a poison to a restricted site of action in the insect have encountered considerable difficulties. Histological examination of poisoned insects, where the organs are fixed and stained, does not bear the same validity as observation of living tissue. Thus the detection of histopathological change in certain organs of insects taken just before death is open to the criticism that the basic action of the poison has already occurred and the lesions are an effect rather than a cause of the metabolic derangement.

Definite histological change has been consistently detected in the mid-gut epithelium of insects that have ingested arsenate, arsenite, fluoride and fluosilicate. Since these cells are essential for the processes of digestion and absorption, it is valid to assume that the death of the insect is a direct consequence of their destruction. Moreover the lesions occur even if the arsenite is administered by injection into the haemocoele. Similarly the appearance of histological changes, particularly in the brain and

ganglia of insects treated with nerve poisons such as pyrethrins and thiocyanates, does at least indicate that these tissues are preferentially attacked and are a true site of action.

The immediate cause of derangement, however, cannot be indicated by histological methods, but its determination requires either the methods of experimental physiology to show where and how the poisoned animal or tissue behaves abnormally, or the techniques of biochemistry to elucidate what biochemical processes have been most adversely affected. The initial pathological changes in nerve fibres, which involve the decay of the ultrastructure of their cytoplasm and sheaths, may be detected by examination under polarized light.

The establishment of a single basic mode of action of certain poisons may be impossible, since life processes are so numerous and interdependent. For the pathologist, precision is attained with visible change in certain cells and tissues; for the physiologist, with impairment of function in certain life processes; and for the biochemist, with inhibition of certain enzyme systems and individual enzymes.[7] Evidence of enzyme inhibition is not necessarily final, since it is obtained from preparations in which the enzymes have been torn out of their normal position in the architecture of nucleus, cytoplasm, or cell wall. Only a small fraction of the surface of biocatalysts, for example those of the cell membrane, is operative in nature. Precision is attained with the discovery of the active radical or grouping, the lock into which the key of the substrate fits and is thereby activated. On this basis, a metabolic poison may be regarded as a foreign key which also fits the lock and thus denies its use to the normal metabolite.

Symptomatology of insecticides

The basis of a pharmacological classification of insecticides is an accurate characterization of the symptoms induced by them. The objective of discovering symptoms in insects which are characteristic of a particular compound or group of organic homologues has proved extremely hard to attain. The nature of the insect, whether for example it is a sluggish larva or an active adult, may have as much bearing on the symptomatology as the poison itself. The mode of entry of the poison is also a

material factor, since the fast action of fumigants and of contact applications stands in sharp contrast to the slow process of poisoning by insecticides added to the food.

From observation of the symptoms evoked by them, fumigants may be divided into narcotic and irritant poisons. The narcotic vapours, such as CCl_4, CS_2, and HCN, are characteristically liposoluble; the irritant poisons, such as chloropicrin, methyl bromide, and SO_2, are considered to release acid in the tissues. Certain contact insecticides, such as the thiocyanates and pyrethrins, also induce a narcosis or knockdown of the insect. Just as the symptoms shown by insects under the influence of narcotic fumigants closely resemble the symptoms of anoxia, so the clumping of the nuclear chromatin in the nerve cells of insects narcotized by oils or pyrethrins is also a result of anoxia.

Nerve poisons characteristically induce the appearance of symptoms in four stages: excitation, convulsions, paralysis, and death. The narcotic fumigants show typically only the three stages of excitation, paralysis, and death, the convulsions or spasms being omitted. With the irritant vapours the stage of paralysis also is lacking. The paralytic stage induced by the contact nerve poisons may be either (i) a flaccid paralysis where the muscles are relaxed, as with rotenone poisoning, which is analogous to narcosis; or (ii) a tetanic paralysis where the muscles are immobilized in a contracted position, as in DDT poisoning.

Another basis for a system of symptomatology is afforded by a study of the respiration of poisoned insects (Fig. 1). In the intact and unrestricted insect this respiratory picture is largely a measure of the amount of muscular action consequent on excitation or narcosis as the case may be. The most extensive investigations have been carried out on *Blattella*,[56] *Oryzaephilus*,[116] and *Tribolium*.[113a] Nerve poisons such as DDT, methoxychlor, lindane, PDB, TEPP, dichloroethyl ether, pyrethrins, nicotine, azobenzene, and the dinitro compounds all cause a marked and immediate increase in oxygen consumption under these conditions. In the case of toxaphene, chlordane, heptachlor, aldrin, dieldrin, and parathion this increase is preceded by a latent period of 30 min to 6 hr during which the insect remains passive. Hydrogen cyanide and the thiocyanates (*Lethanes*) cause an

immediate and progressive depression of respiration; in the case of rotenone and ryania this depression is preceded by an initial slight rise. Sabadilla has no effect beyond a slight initial increase, while phenothiazine does not affect the respiratory rate at all. When paralysis sets in, the oxygen consumption falls in all cases, while the production of carbon dioxide continues at an unchanged or increased rate, resulting in high respiratory quotients. In comparison of initial effects it is important that the dosage be set at a comparable level in terms of the median lethal dosage for the particular poison.

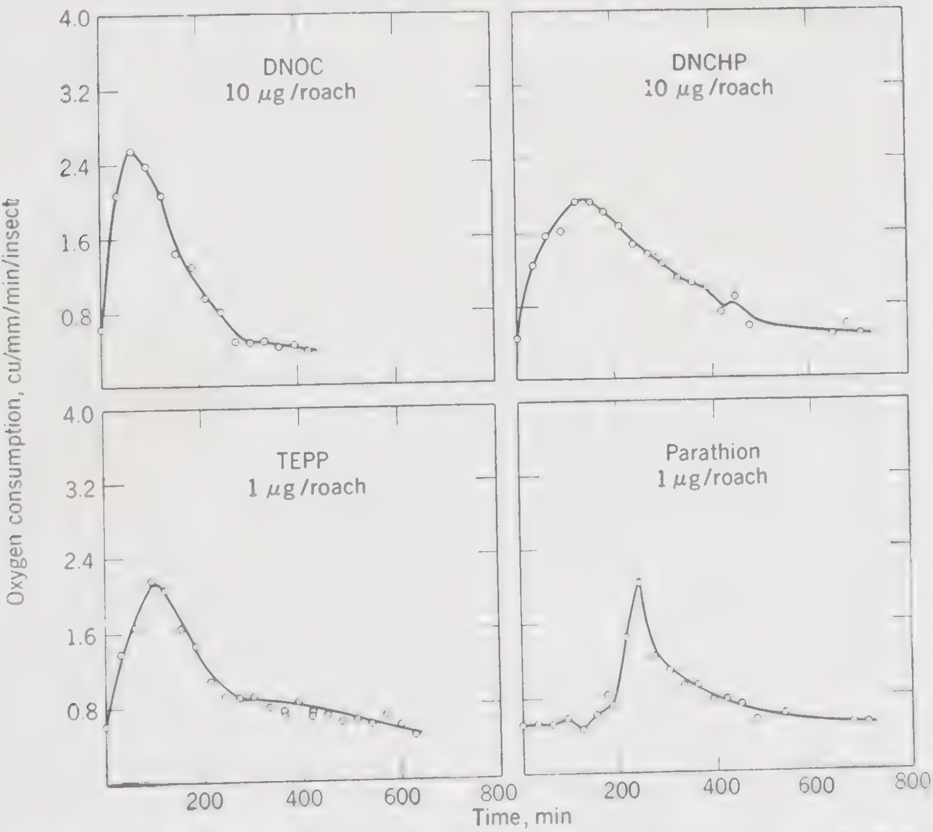


FIG. 1. Rate of oxygen consumption by *Blattella* injected with DNOC, DNCHP, TEPP, or parathion. (From Harvey and Brown)

Heart action. The automatism of the insect heart has been considered to be probably myogenic, since it may continue to beat after the death of the insect, or after it has been separated

from the ventral nerve cord or even cut into pieces; and many species have no detectable innervation. However, the rate and amplitude of beat are under nervous control.[220a] Although no specific cardiac centre was demonstrable in *Melanoplus*, the nerve drugs acetylcholine and atropine were found each to exert their characteristic effects.[40,76] Since the heart of *Periplaneta* is accelerated by acetylcholine and paralysed by atropine, there is probably a cholinergic accelerator; since it is stimulated by adrenalin and blocked by ergotamine, it is probably controlled by an adrenergic pacemaker. But there is a difference from the mammalian heart in that digitalin stimulates and caffein inhibits the insect heart.[108a]

Insecticides have a far greater effect on the heartbeat of the intact insect than on that of the decapitated insect [142] or the isolated heart. The nerve poison anabasine, for example, is found to evoke a fourfold increase in heartbeat when the nerve cord of *Pteronus* (*Nematus*) is intact, and a lesser but nonetheless significant increase when it is severed.[182] Nicotine,[108a] parathion, and the dinitro compounds increase the pulsation rate. But DDT has no effect on the isolated heart of *Stenopelmatus*,[40] or on the heart of decapitated *Periplaneta*.[142] Other chlorinated hydrocarbons had little effect beyond a very slight acceleration.

With the contact application of nerve poisons such as pyrethrins or nicotine, the appendages and peripheral parts of an insect such as the roach are paralysed long before the heart stops.[35] When a narcotic fumigant such as CCl_4 or CS_2 is applied to aphids (*Macrosiphum tulipae*), body paralysis is complete within 1 min, but the heart may continue to beat for 15 min; with a non-narcotic fumigant such as nitrobenzene or formaldehyde, the heart does not stop for almost 1 hr after paralysis has set in; [105] with the venom of solitary wasps, the heart continues to beat indefinitely in the paralysed victim. In *Ephestia* larvae subjected to carbon tetrachloride, a sudden increase in heart rate precedes a steady deceleration. But any materials which reduce the rate of respiration, such as hydrogen cyanide, rotenone,[142] and the thiocyanates, also decrease the frequency of heartbeat.[35]

A great number of chemicals have been found upon injection to effect a change in the rate of heartbeat, to destroy the synchronization of the wave of contraction, or to cause a reversal of the

direction of beat.[235] In some cases the heart may be occasionally stopped, to resume after a short period. Complete arrest of the heartbeat has no immediate effect upon the insect.[94] The chlorinated hydrocarbon insecticides and the organic phosphates have comparatively little effect on the heartbeat. The insecticides which exert the most effect on the heart of the intact cockroach are rotenone, which gradually slows this organ; and the dinitro compounds, which initially stimulate and finally arrest it suddenly.[142]

Nerve conduction. Most of the powerful new insecticides are nerve poisons, and their effect may be studied by perfusing them over the isolated nerve cord or individual nerves of arthropods. The conduction of nerve impulses is accompanied by a wave of polarization which passes along the nerve, the stimulated area being negative with respect to the adjacent areas. The depolarization of the stimulated area involves an action current, which may be detected by amplifying it and projecting it by a cathode-ray oscillograph onto a moving film. The depolarization will be visible as a number of spikes on the film record, each of which represents a drop in potential or polarization. The greater the stimulus, the greater the polarization, and the greater the consequent depolarization, and thus the higher the spike on the oscillograph record.[89] It should also be noted that the nerves of living insects (e.g. the ventral cord of the roach) show action currents with occasional bursts of spikes even when they are not being stimulated[179] (see Fig. 16).

The depolarization, or the drop in potential, of nerve involves an increase in the permeability of the nerve sheath, to allow the entry of positive K ions to depolarize the negative potential. The increase in permeability may be connected with the release of free acetylcholine from its bound form; the acetylcholine must then be destroyed by the enzyme cholinesterase as soon as it has performed its function.[2] A reduction in the amount of K available for depolarization has an excitatory effect on arthropod nerve. If acetylcholine is withheld from crayfish nerve, the absence of K is no longer excitatory.[175]

In the physiology of nerve, calcium ions are antagonistic to potassium ions. The addition of Ca ions to the perfusate of crayfish nerve is equivalent to the removal of K ions. In the living

cell, it has been established that Ca (or Mg) ions decrease the permeability of the membrane, whereas K (or Na) ions increase it. High concentrations of Ca have a stiffening effect on the cytoplasm.[89]

Pharmacology of insect nerve. Evidence is accumulating to show that the central nervous system of the insect is physiologically different from that of the mammal. Instead it closely resembles the parasympathetic autonomic system of vertebrates; here the synaptic transmission of nerve impulses depends on the mediating effect of acetylcholine, which must be destroyed immediately after use by the action of the enzyme cholinesterase.

Eserine (physostigmine), which is an inhibitor of cholinesterase, is a stimulant for the vertebrate parasympathetic system. Similarly its effect on the physiology of *Mantis* or *Periplaneta* is to induce great excitation and high muscle tonus, and high doses cause instantaneous spasm and immobility. These insects respond in the same way to pilocarpine, which is another parasympathetic stimulant.[173] Nicotine, eserine, or pilocarpine was found to stimulate action currents in isolated cockroach nerve, and high concentrations of the first two drugs blocked them altogether. Preliminary treatment with atropine prevented the stimulant effect of pilocarpine on insect nerve, an effect similar to that observed in the cholinergic nerves of the vertebrate parasympathetic system.[179]

On the other hand strychnine, a stimulant for the vertebrate central nervous system, was found to be a depressant for insects, since on injection into the head of *Mantis* it caused loss of muscle tone and paralysis of the head appendages.[173] Adrenalin, histamine, and curare have no effect on insects when applied in the low doses which elicit marked response in the mammal,[131, 165] although in higher concentrations adrenalin and strychnine, as well as picrotoxin and camphor, were found to be excitatory for *Automeris* and *Melanoplus*.[38, 39]

The nerves of insects are morphologically and biochemically similar to those of the vertebrate parasympathetic system. The myelin sheaths of the nerve cells of *Apis* were found to resemble parasympathetic nerve not only in their thinness but also in the chemical properties of the lipoids which they contain.[185] The entire brain of *Apis* has a high content of kephalin, with some

lecithin, sphingomyelin and sterol; it resembles premedullated nerve of young vertebrates in lacking any cerebroside.[145a]

The central nervous system of an insect such as the cockroach contains a very high concentration of acetylcholine. In resting nerve there is about twice as much acetylcholine in bound form as there is free, but during activity the concentration of free acetylcholine rises to approximately 200 μg gm of tissue.[133]

The concentration of the enzyme cholinesterase in the central nervous system of the bee or roach is extremely high, and there is about half as much in peripheral nerve. The enzyme resembles the true cholinesterase of vertebrates in hydrolysing acetyl-β-methylcholine,[7] but differs from it in hydrolysing this derivative three times as fast as acetylcholine itself.[166] It is poisoned by eserine but is unaffected by nicotine or curare. Most of the insecticides studied, including DDT and thiocyanates, were found not to inhibit the enzyme. Sodium fluoride and the organic phosphates are the only insect poisons whose anticholinesterase activity has been demonstrated, with the exception of the derivatives of phenothiazine.

It might be expected that acetylcholine itself would be a powerful nerve poison for insects, since its end result would be the same as that of an anticholinesterase. However, it has proved to be ineffective on injection into the insect or on perfusion over nerve cord, requiring high concentrations even to show its stimulating effect. It is possible that the impermeability of nerve sheaths to this substance may protect the nerves themselves from its powerful mediatory action.[179, 211]

In the following pages descriptions of the gross symptoms of the intact animal under the influence of particular poisons will be given; although they are indefinite they are the accompaniments of death on application of the insecticide, and to them all data of a more exact and restricted physiological nature must ultimately be applied.

Heavy metals

The use of heavy metals for insect control is limited by the hazard it involves to other forms of life since they are general protoplasmic poisons. The most important are the salts of mercury (calomel and corrosive sublimate) and of copper (Paris green

and cuprous cyanide). Their mode of action presumably involves the precipitation of proteins and the inhibition of their enzymic properties. The kinetics of poisoning by heavy metals would indicate that a process of adsorption rather than chemical combination is taking place.[31]

The metallic radical of arsenical salts is considered to be of secondary importance although the particular metal has a modifying effect on the efficacy of the salt. The stomach toxicity of the arsenates and arsenites falls in the following order: [149]

$$\text{Arsenates: Pb} > \text{Cu} > \text{Ca} > \text{Mg} > \text{Zn} > \text{Fe}$$

$$\text{Arsenites: Mg} > \text{Cu} > \text{Ca} > \text{Pb} > \text{Fe} > \text{Zn}$$

The lead in lead arsenate does not add to the toxicity of the salt, which is due to the arsenic alone.[212] It is considered that it may not be absorbed by the alimentary canal; when *Bombyx* larvae are fed lead arsenate, the lead in it is nearly all excreted within 24 hr.[25] Many instances have been reported of insects boring in lead pipe and cable as if it were an entirely non-toxic material. Ingestion of lead oxide, or of iron or manganese oxide, has only a slight depressant effect on the respiratory rate of *Leptinotarsa*.[57] Paris green (copper acetoarsenite) differs from the other arsenicals by causing little or no damage to the mid-gut epithelium.[153]

Mercuric chloride applied to the cuticle of *Passalus* was observed to precipitate the proteins of the underlying hypodermal cells.[157] When added to the ground tissues of this beetle, it effected complete inhibition of the catalase and dehydrogenase activity.[158] Oral poisoning of *Blatta* by mercuric chloride causes a drastic decrease in the haemocyte count.[60] The vapour of elemental mercury has been found to penetrate insect eggs and disintegrate the cytoplasm and nucleus of the embryonic cells; [100] it has a similar effect on the young larvae of *Bruchus*,[71] but it is innocuous to the adults of insects affecting stored grains.[229]

Acids

Fatty acids. The lower fatty acids, such as acetic acid, are weak contact insecticides despite being capable of a limited cuticular penetration. If acetic acid is injected, however, it is

highly toxic; it has been found to gelatinize the alimentary canal and Malpighian tubules of aquatic dipterous larvae.[1] Its toxic action is considered to be due to the disruption of the cell membrane and coagulation of the cytoplasmic proteins.[135]

Formic acid and its esters are more toxic as fumigants than acetic acid and alkyl acetates. The volatile methyl esters of the lower fatty acids have proved to be irritants to scale insects.[156] Vapours of lower fatty acids have the property of inhibiting the normal coagulation of the haemolymph which occurs on exposure to air.[192] The dibasic oxalic acid is a poison also for insects, presumably because of its power of removing tissue calcium by precipitation;[149,187] it may be noted that certain insects normally excrete calcium oxalate.

The higher fatty acids are enabled to show contact toxicity by virtue of the lipoid solubility of their hydrocarbon chains. Capric acid or lauric acid, the most effective of the series, completely paralyses *Anuraphis* almost immediately.[191] The scale insect *Phenacoccus* is quickly immobilized and killed by immersion in coconut fatty acids or oleic acid.[44] The sodium soaps are more insecticidal than the free fatty acids since they enhance the toxicity of the fatty acid radical.[46,194]

It is considered that the acidic carboxyl group is responsible for the toxicity, and that all members of the series would have similar contact activity were it not for the fact that the length of the side-chain dictates their ability to penetrate the cuticle. Thus the lower fatty acids such as caproic proved not to penetrate into *Calliphora* larvae since their carboxyl group is retained by chemical reaction in the cuticle, whereas the higher analogues such as lauric acid are carried through the integument by the liposolubility of their long apolar hydrocarbon chains.[97] On the other hand, it was noted that the only fatty acids to show significant body-wall penetration of *Blattella* were acetic and butyric acids.[135]

Fatty acids have been observed to inhibit both dehydrogenase and phenoloxidase activity of *Tenebrio* and *Musca* larvae, even when applied in low concentrations. It has been suggested that they react with basic radicals in the protein-enzyme complex.[98]

Mineral acids. Because they dissociate freely, mineral acids have difficulty in penetrating the insect cuticle. Thus they have

no place as contact insecticides, in concentrations that are practical to apply. However, it is considered that certain fumigant vapours release mineral acids in the tissues and that these acids are responsible for the toxicity of the vapours. Cyanogen chloride, phosgene, and chloropicrin show the same symptomatology in insects as hydrochloric acid itself.[155] Chloropicrin penetrates the body wall and tracheae of insects very rapidly [135] and has a fast knockdown effect.[199] A number of unsaturated alkyl and aryl halides, such as benzyl chloride and bromide, allyl bromide and bromobenzyl cyanide, and aldehydes and ketones such as benzaldehyde and acetophenone, exert an irritant effect on insects which may or may not be accompanied by toxicity.[155] These compounds have an irritant effect on the lungs and a lachrymatory effect on the eyes of mammals.[216]

It is possible that methyl bromide, which is an irritant and highly penetrative fumigant, may also be classified in this category. It does not induce narcosis, and insects appear to be fully active after a 5-hr exposure; death occurs in 48 hr.[190] Methyl bromide has been found to oxidize SH compounds, such as cysteine, glutathione, and reduced keratin, and to inhibit those enzymes, such as succinic dehydrogenase and hexokinase, which have sulphydryl groups; it is without effect on cytochrome oxidase.[115]

Sulphur dioxide is also a corrosive poison, possibly because it is the precursor of sulphurous acid in the tissues. It differs in effect from the usual fumigant gases by not causing narcosis of grain weevils for at least an hour.[20] The symptoms of SO_2 poisoning in *Melanoplus* nymphs were found to be characterized by irritability, intensified cleaning movements, ataxia, and paralysis of the posterior legs.[217] The vapour is adsorbed into the body of the insect, where it remains in a stable combination and precipitates the tissue proteins.[187]

Alkaloidal reagents

This group of acidic compounds, which combine with kationic proteins to precipitate them, includes tannic acid and picric acid, which are used as fixatives and exert a moderate insecticidal effect on the living insect. Phenol and the nitrophenols and nitrocresols may be considered under this heading, although it is

realized that protein precipitation constitutes only a part of their pharmacological effect. For instance, the insecticidal effect of carbolic acid is due to its lipoid solubility as well as to its possession of an acid radical. The crude creolin used many years ago, containing phenols and cresols, was found to disintegrate the fat body and muscles of caterpillars at the particular points where it was applied.[187]

In the nitrophenols and nitrocresols we enter a group which exert a pronounced effect on metabolic processes. They are known to increase the carbohydrate breakdown in isolated mammalian tissue and to increase both carbohydrate and fat metabolism in the intact animal.[76] Both 2,4-dinitrophenol and 3,5-dinitro-*o*-cresol (DNOC) notably increase the rate of respiration in the developing and diapause embryo of *Melanoplus differentialis;* high concentrations of these nitro compounds completely inhibit respiration. Their effect depends on the cells being intact, and is most marked in an acidic medium where their dissociation is at a minimum. Since the stimulating effect of these dinitro compounds is cancelled by cyanide and carbon monoxide, it is probably connected to the cytochrome oxidase system. Moreover the 25% increase in respiration is accompanied by an abnormal production of ammonia, which suggests an oxidation of protein rather than carbohydrate in the treated embryos.[12] From experiments on yeast, it appears that DNOC accelerates the acceptance by cytochrome *c* of hydrogen from the substrate, and that free SH groups are necessary for its action.[108] Marked stimulation of oxygen consumption has also been observed in *Galleria* larvae poisoned by 2,4-dinitrophenol.[37] A 50% increase of oxygen consumption was shown by honeybees fed DNOC at a level of one-sixth of the median lethal dose; similar results were obtained with DNCHP.[69] A high initial increase of respiratory rate followed by a rapid fall has also been observed with DNOC in *Oryzaephilus* and *Tribolium*,[112] and with DNOC, DNCHP, and DNBP in *Blattella* [86] (Fig. 1).

When dusts containing *o*-nitrophenol, *p*-nitrophenol, or 2,3-dinitrophenol were applied to *Dendrolimus* or *Panolis*, the larvae responded with rapid movements and contortions, sometimes accompanied by excretion from mouth and anus, followed by a quick knockdown.[181] The high speed of action is characteristic

of the insecticide DNOC, whose effects on *Lymantria monacha* larvae appeared 1 min after application of the dust. The succession of symptoms involved (i) restlessness, (ii) convulsions, i.e. writhing, (iii) paralysis, and (iv) death after 30 to 45 min: the picture is suggestive of a nerve poison.[92] Cockroaches (*Periplaneta* and *Blattella*) sprayed with DNOC showed exaggerated irritability on stimulation, and fine tremors of the appendages preceded death. When either DNOC or DNCHP was injected into the intact *Periplaneta*, the rate of heartbeat was steadily increased until the heart finally stopped, usually within 1 hr[142] (Fig. 2).

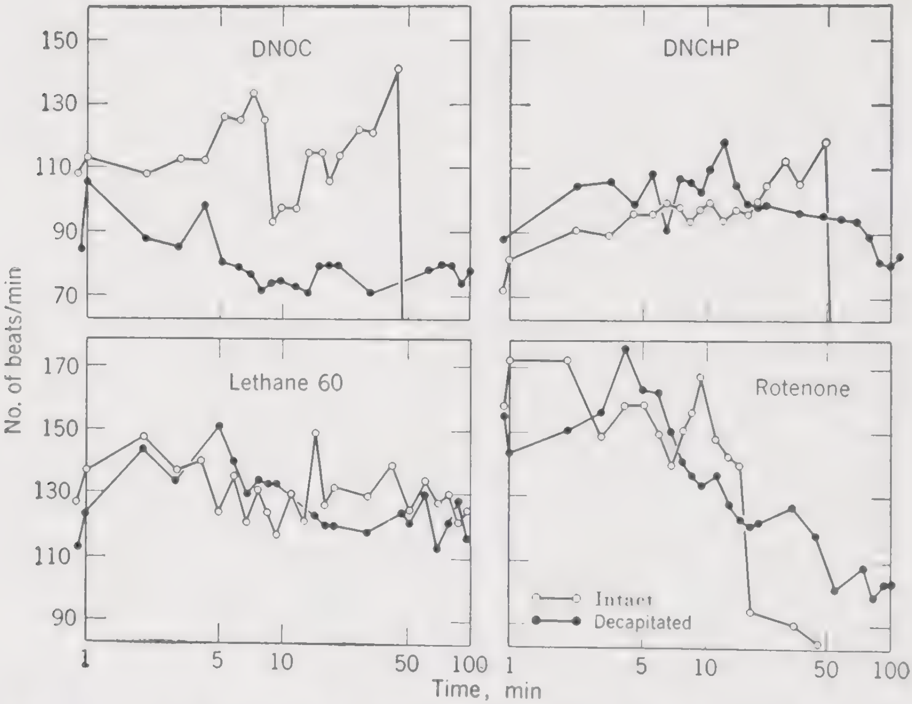


FIG. 2. Rate of heartbeat of *Periplaneta* injected with DNOC, DNCHP, Lethane 60, or rotenone. (From Orser and Brown)

DNOC is highly poisonous to all insects, even if they are as heavily sclerotized as weevils are, and to eggs and pupae as well as to larvae and adults. It has been found that insect cuticle will adsorb DNOC out of solution in water or oil, just as other nitro dyes "take" on materials steeped in them. The adsorbed DNOC has been shown to migrate along the cuticle; if only half

a butterfly wing is dipped into the solution, the colour will spread to the other half. Experiments on mushrooms have demonstrated that DNOC penetrates the structural chitin and precipitates the protein in the underlying cells. It is considered that the same process may take place in the cuticle and hypodermal cells of insects. The superiority of DNOC to picric acid as a vital fixative is attributed to its much greater liposolubility affording it more ready access to the deeper tissues.[198]

Oxidizing and reducing substances

A number of compounds have been used as insecticides presumably on the basis of their effect on the oxidation-reduction potential on entering the insect. The oxidizing agents include permanganates, chlorates, and peroxides, and reducing agents include hypochlorites, nitrites, and sulphides.[212] Of these only the sulphides derived from lime-sulphur have achieved extensive practical application.

The calcium polysulphides of lime-sulphur evolve hydrogen sulphide for 6 hr after the application, but this has been shown to be insufficient to account for the mortality of *Aspidiotus* scales. It appears that the spontaneous oxidation of the sulphides absorbs the atmospheric oxygen at a sufficient rate to prevent its reaching the insect, which dies after some 18 hr.[139] Hydrogen sulphide has appreciable fumigant toxicity to insects, and its penetration to all tissues of the body has been demonstrated by addition of lead acetate to the dissection.[187] The toxic action of H_2S is due to its inhibiting cellular respiration as a consequence of its combination with the Fe in cytochrome oxidase.[5, 149] Hydrogen sulphide has also been found to inhibit the digestive protease of grasshoppers.[186] It should be pointed out, however, that SH compounds are valuable as activators of intracellular proteases such as cathepsin, and this effect on the oxidation-reduction potential is important for a number of cellular enzymes.[205]

Formaldehyde and ethylene oxide

Formaldehyde is a strongly reducing material, which is also a protoplasmic poison because of its ability to combine with the free amino groups of tissue proteins. Its effect on insect tissue

preparations resembles that of mercuric chloride in strongly inhibiting catalase and dehydrogenase activity.[188] The fact that formaldehyde vapour taken in by the insect can be exhaled again would indicate a process of solution rather than adsorption.[187]

The symptoms of formaldehyde poisoning in the housefly have been described as a progressive paralysis, spreading forwards from the metathoracic legs to the wings and finally the mouthparts. As opposed to narcotics, there is no recovery from poisoning by formaldehyde taken by mouth.[90]

The effects of ethylene oxide vapour are very slow in developing. Insects fumigated by it appear quite normal, but they die several days later. It is considered that this long latent period involves its conversion in the body either to formaldehyde,[149] or, by way of ethylene glycol, to oxalic acid.[20]

Inorganic acid radicals

These are the fluoride, fluosilicates, and fluoaluminates, the borates, arsenites, and arsenates. They have been extensively applied as stomach insecticides, although they also show moderate contact toxicity. Insects which have ingested these inorganic acid materials characteristically exhibit lesions in the epithelium of the mid-intestine.

Arsenical compounds. The oxides, acids, and salts of arsenic are applied primarily as stomach insecticides, although they are capable of limited contact action.[113] Larvae of *Prodenia eridania* poisoned by ingestion of lead arsenate show the following symptoms: they refuse to eat further, usually regurgitate, and become inactive; after a period in which some individuals become temporarily activated, they die quietly without convulsions.[227] Nymphs of *Blatta* orally poisoned by arsenious oxide pass watery faeces, their movements become feeble, and finally they become motionless except for spasmodic twitching of the appendages on stimulation.[60]

Injection of arsenites or arsenates into *Periplaneta* results in the appearance of symptoms which have been carefully described in the following succession: *A*, decrease in activity; *S*, loss of equilibrium; *L*, loss of recovery reflexes; M_1, general asthenia; M_2, very weak movements on stimulation; *D*, no responses. The successive stages may be plotted against the time

of their appearance in such a way that the course to death may be represented as a straight line.[137] The arrangement of the stages on the ordinate may serve to plot similarly the symptoms resulting from other insecticides, and the resulting time graph may be compared with the straight line for arsenicals (Fig. 3).

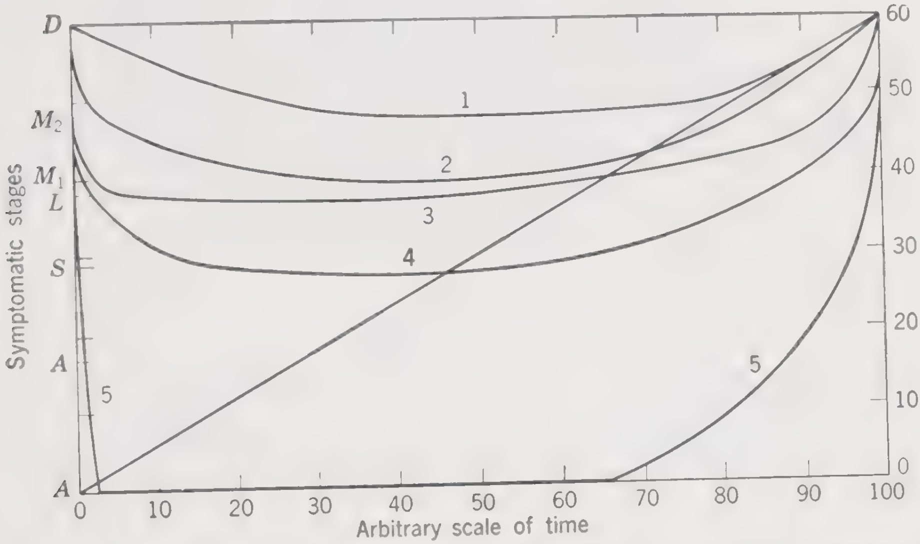


FIG. 3 Development of symptomatic stages in *Periplaneta*. *Diagonal straight line*: injected with sodium metarsenite. *Curves 1 to 5*: injected with decreasing concentrations of sodium cyanide. (From Munson and Yeager)

If larvae of *Prodenia* are taken 3 hr after oral poisoning with lead arsenate, while they still show feeble movements, histological examination shows that the epithelial cells of their mid-intestine are disintegrating. The striated border and cell walls fade away, vacuoles appear in the cytoplasm, and the chromatin of the nucleus becomes clumped, dispersed, or dissolved. Similar histological damage may be detected as a response of these larvae to calcium arsenate, arsenious oxide, or calcium arsenite; Paris green, however, causes only slight histopathology.[227]

These pathological symptoms have also been found in larvae of *Vanessa* and nymphs of *Locusta* poisoned by ingestion of sodium or calcium arsenite. Here, again, Paris green did not show these effects. Larvae of *Lymantria* or *Pieris* were considerably more resistant to tissue damage. Agglomerations of

brown material have been detected in the vacuoles appearing in the gut cells of *Vanessa*[153] (Fig. 4). The cell degeneration has

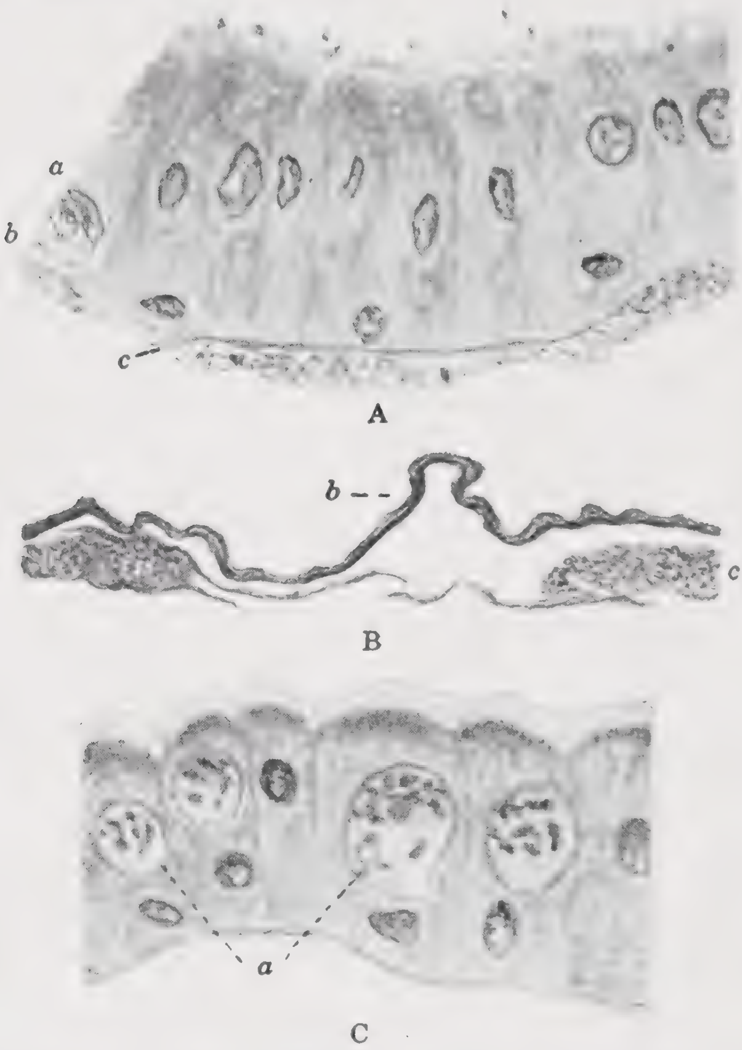


FIG. 4. Effect of calcium arsenite on intestinal epithelium of *Vanessa*. A. Normal condition: *a*, epithelium; *b*, connective membrane; *c*, circular muscle. B. Severe poisoning by Ca arsenite: the epithelium is completely removed from the membrane. C. Mild poisoning by Ca arsenite: the epithelium contains vacuoles with inclusions of a brown substance, *a*. (From Pilat, courtesy of Commonwealth Institute of Entomology)

been described as a process of necrosis, and it is followed by desquamation of the cells.[146] In *Locusta*, although mild doses initially effect an increase in cell division, heavy doses cause

large areas of epithelium to separate from the basement membrane, a process which may be partially attributed to plasmolysis. The desquamated cells pass down the alimentary canal and are digested, leaving the basement membrane cleaned of its epithelium.[153]

Oral poisoning by arsenious oxide (or by sodium fluosilicate) reduces the haemocyte count of *Blatta* from 35,000 to 7,000 per cubic millimeter, and the larger cells are entirely eliminated.[60] A similar effect is obtained in *Locusta*, where the haemocytes have been detected in process of disintegration, while the production of new and smaller haemocytes is indicated by the frequency of mitotic figures (Fig. 5). Very small cells (4 μ in diameter), which are one-half the size of the smallest normal cells and have a dense nucleus and little cytoplasm, make their appearance.[154] Contact application of sodium arsenite to *Schistocerca* also causes cell division, vacuolization, chromatolysis, and breakdown of cell walls.[113] Stomach poisoning of the grasshopper *Calliptamus* with sodium arsenite results in the appearance of abnormally large blood cells in addition to these changes.[186]

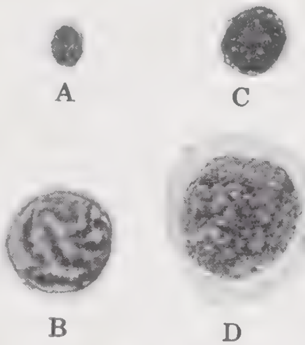


FIG. 5. Effect of calcium arsenite on haemocytes of *Locusta*. A, B. Small poisoned cells. C, D. Normal small cells. (From Pilat, courtesy of Commonwealth Institute of Entomology)

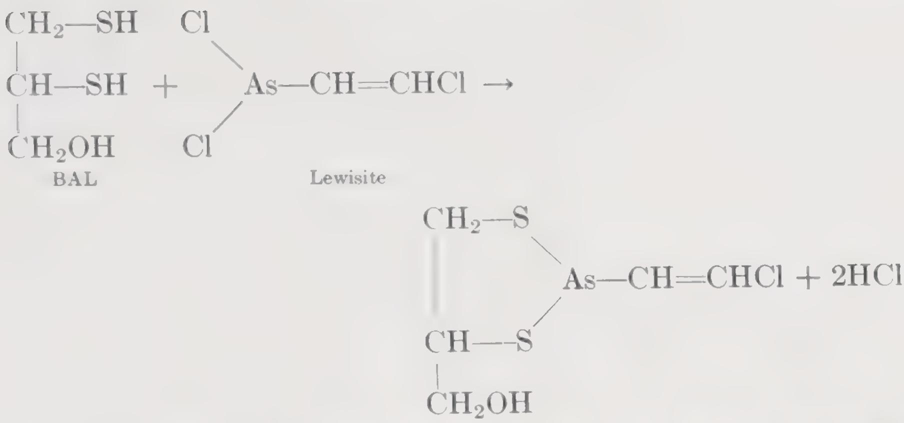
The general blood picture resembles the response to bacterial infection. The interpretation may be derived that the haemocytes serve as traps for the encystment or neutralization of arsenicals. Indeed, if they are previously loaded with foreign bodies such as carbon particles, the susceptibility of the insect to sodium arsenite is found to be considerably increased.[231] This discovery, made with *Periplaneta*, was found to apply also to sodium fluoride, but not to nicotine or pyrethrum poisoning.[123] Another effect of arsenicals is a loss in blood volume,[140] presumably as a consequence of alimentary hypersecretion,[34] reflected in the characteristic symptoms of regurgitation and watery faeces. In addition, a pronounced drop in the concentration in

the blood of the non-protein nitrogen fraction, of which the most important constituent is amino acid, was noted in cockroaches poisoned with sodium arsenite.[94] Ingestion of sodium arsenite by *Bombyx* decreased the rate of heartbeat; injection caused an immediate increase.[23]

It would appear that arsenicals have no more inhibitory effect on insect digestive enzymes than on mammalian, since potato beetles poisoned by lead arsenate or Paris green were found to have their digestive enzymic activity unimpaired.[59] Similarly the enzymes of the Malpighian tubules—oxidase, peroxidase, and protease—are unaffected by arsenic, nor is their ability to excrete salts (including arsenicals themselves) impaired by the poison.[146] However, histological changes have been noted in those parts of the Malpighian tubules which are appressed to the alimentary canal, where also the intestinal muscle layers are affected.[143]

In *Prodenia*, lead arsenate poisoning is accompanied by deposits of black spots in the cells of the epithelium and in the muscle. Since they do not develop on administration of other salts of lead (the acetate, chromate, or nitrate) they have been considered to be insoluble sulphides resulting from the combination of arsenic with the SH groups in glutathione and the cytoplasmic proteins.[227] In view of the success of glutathione and cysteine in protecting both rats and trypanosomes against arsenite poisoning, it was suggested that the normal SH groups in the tissues were the specific receptors for arsenite ions.[213, 214] In many species of insects it has been found that arsenical poisoning decreased the free SH groups in the tissues by an amount between 20 and 80%.[58]

In vertebrate tissues, especially the brain, sodium arsenite has been found to inhibit the pyruvate oxidase system that is necessary for the completion of carbohydrate breakdown. It was concluded that the trivalent arsenic combines with the free SH groups of the enzyme. If a dithiol compound such as 2,3-dimercaptopropanol was administered, its SH groups competed successfully for the arsenic and removed it from further action in a stable ring combination. This compound, termed BAL (British Anti-Lewisite) is able to remedy the skin lesions and other symptoms caused by trivalent arsenic in such poisons as lewisite.[illegible]



It is considered that salts of copper, mercury, and lead also inactivate a number of enzymes by combination with their free SH groups. Selenium inhibits succinic dehydrogenase, and mercury may inhibit cholinesterase, in this manner.[7] The remedial effect of BAL on these cases of metallic poisoning has been actively investigated.

In many cases there is a considerable divergence in toxicity between the trivalent arsenite and the pentavalent arsenate. Whereas arsenite is found to poison the oxidative decarboxylation of pyruvic acid in carbohydrate breakdown, arsenate is not an enzyme inhibitor and indeed may partially replace phosphate in the normal process of carbohydrate breakdown in yeast.[5] For many insects, such as *Malacosoma* and *Datana* caterpillars, the arsenate is much less toxic than the arsenite.[22] And arsenic oxide (or sodium arsenate) was found to be 60% less depressant on the respiratory rate of *Leptinotarsa* than arsenious oxide (or sodium arsenite).[57] However, for other insects such as the honeybee [22] and the migratory locust,[143] the arsenic administered as arsenate is almost as toxic as it is in the form of arsenite. It is generally considered that, in order that arsenical poisoning may occur, arsenates must first be reduced to arsenites. The toxicity of arsenates may be increased by the addition of sulphite or zinc dust in order to assist their reduction.[212]

Larvae of *Leptinotarsa* poisoned by arsenite or arsenate were found to show a significant decrease in oxygen consumption and a consequent rise in the respiratory quotient.[57] Isolated muscle or fat body of *Carpocapsa* larvae treated with sodium arsenite

showed a drop in oxygen consumption of 30–50%.[72] Tissues of three insect species poisoned by arsenite exhibited various degrees of loss of dehydrogenase activity, as measured by their ability to reduce methylene blue.[195] The dehydrogenases of the mid-gut of *Calliptamus* were almost completely inhibited by sodium arsenite.[186]

However, the interspecific differences in susceptibility of the three species (*Locusta, Pieris, Euxoa*) to arsenic poisoning are not proportionate to their relative susceptibility to loss of dehydrogenase activity. Moreover, whereas adult *Periplaneta* may be killed by arsenious acid in a few minutes, their respiratory rate decreases only gradually over a period of hours. It may be concluded that although reduction of tissue respiration does occur with arsenic poisoning, it does not have a direct bearing on the killing process, but is only incidental to it.[144] The toxicity of arsenic is considered to be primarily due to tissue disintegration and protein precipitation, which require quite large doses for their production.[212] At the lower dosage levels characteristic of an enzyme poison, arsenic is harmless and may even have a chemotherapeutic effect for caterpillars.[197]

When arsenite was added to *Carpocapsa* tissues above a concentration roughly equivalent to the calculated body-fluid concentration for a decisive lethal dose, further increase in arsenite was found to decrease the degree of inhibition of the respiratory enzymes.[72] This point of inflection in the concentration-effect curve was also noted on consideration of the survival time of *Periplaneta* and *Blatta* injected with sodium metarsenite ($NaAsO_2$) and sodium monohydrogen orthoarsenate (Na_2HAsO_4). This effect was considered to be due to the fact that at higher concentrations the proportion of arsenic in the form of the toxic AsO_2^- ions was less than at the lower concentrations, where fixation of ions by the tissues was evoking greater dissociation.[234] The inflection in the concentration-effect curve for *Carpocapsa* tissues was in this case attributed to the formation of an interfacial film of water on the catalytic surfaces.[72]

Fluorides, fluosilicates, etc. The symptoms induced in the cockroaches *Periplaneta* and *Blattella* by contact application of sodium fluoride occur in the following succession: (i) uneasiness

and irritability, (ii) torpor, with sudden nervous starts, which (iii) gradually decline to death. Similar symptoms are shown by borax (sodium borate), and both insecticides lead to death within 4–48 hr after exposure of the insects to the dust.[188] When sodium fluoride is administered in their food, larvae of *Prodenia* show the following symptoms: rearing of head and thorax, turning onto the back, twisting from side to side, and occasional regurgitation. After eating the food poisoned with cryolite (sodium fluoaluminate) or barium fluosilicate, these caterpillars become sluggish, only occasionally showing spasms, and they die while in a flaccid condition.[227]

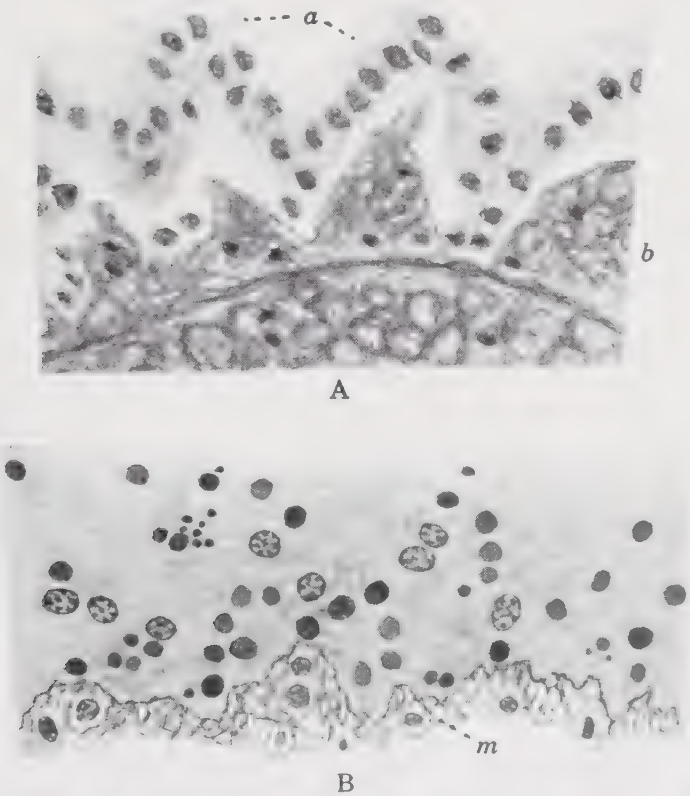


Fig. 6. Effect of sodium fluosilicate on intestinal epithelium of *Locusta*. A. Exfoliation of epithelium, *a*, from underlying connective membrane, *b*. B. Disintegration of epithelium (above) into a continuous mass with coarse-grained or compact nuclei partly breaking up into isolated clumps; *m*, connective membrane. (From Pilat, courtesy of Commonwealth Institute of Entomology)

When examined histologically from preparations made before their death, the larvae poisoned with sodium fluoride exhibited a necrosis of the mid-intestinal epithelium, in whose cells both the nucleus and cytoplasm had been disintegrated.[227] Similar effects were noted in *Vanessa* larvae and in nymphs of *Locusta*. Sodium fluosilicate was less potent in exerting these tissue changes, but sufficient doses caused the epithelium of *Locusta* to exfoliate from its basement membrane (Fig. 6A) or to lose its cellular structure and disintegrate into a continuous mass (Fig. 6B). This stomach poison caused no detectable histological change in *Lymantria* and *Pieris*.[153] Nor did barium fluosilicate induce histopathology in any tissues of *Prodenia*.[227]

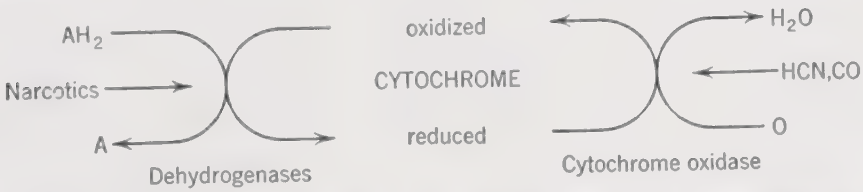
The classical view of the mode of action of fluoride is that it precipitates the calcium necessary for the rigidity of cell membranes.[212] The fluoride ion has been found to inhibit all esterases, including lipases at higher concentrations. Fluoride also inhibits acid phosphatases to prevent phosphorylation of carbohydrate, and phosphoglyceric enolase to arrest carbohydrate metabolism in the triose stage.[7] The affinity of fluoride for metallic radicals also results in its blocking the iron of catalase.[5]

The perfusion of sodium fluoride over the muscle or fat body of *Carpocapsa* larvae was found to reduce both the oxidative and glycolytic activity and to double the respiratory quotient.[72] Addition of fluoride to ground tissue of *Passalus* beetles significantly depressed the catalase activity, but in so doing it slightly increased the dehydrogenase and phenoloxidase activity, whereas borate inhibited the phenoloxidase without affecting the other two types of enzymes.[188] Sodium fluoride has been found to be a partial inhibitor of the cholinesterase of bee or cockroach nerve[166] and of the lipase of the mid-gut of Orthoptera.[186]

Respiratory poisons

There is reason to consider that cellular oxidations in insects are fundamentally similar to those already studied in mammalian tissues, yeast cells, and other types of living matter. Numerous compounds are oxidized by living organisms, and any one of these metabolites, e.g. hexose sugar, passes through several steps in oxidation. Essentially biological oxidation involves the removal of hydrogen from its combination with carbon. Dehy-

drogenation changes the carbon compounds from $—CH_2—$ or $—CHOH—$ to bicarbonate and molecular CO_2. The hydrogen which has been removed is finally accepted by molecular oxygen to form water. However, the simple exchange of H_2 from the metabolite to O requires an intermediate carrier, such as any or all of the three cytochromes, and two enzymes. One enzyme, a dehydrogenase, activates its initial transfer to cytochrome; the other, an oxidase, activates its further transfer to molecular oxygen, leaving the cytochrome free to act again as a hydrogen acceptor.



Cytochrome oxidase (the respiratory ferment of Warburg) structurally resembles the cytochromes, in that it contains Fe in a porphyrin group attached to protein. Thus it is inhibited by the combination of HCN or H_2S with the iron in the molecule. It is also structurally similar to haemoglobin, and thus it is inhibited by the formation of a labile combination with CO analogous to carboxy-haemoglobin. The dehydrogenases, on the other hand, are inhibited by concentrations of narcotics such as urethane and the higher alcohols.[5]

The cytochrome system has proved to comprise some 80% of the cellular oxidation in an insect such as the codling-moth larva.[72] The concentration of cytochrome oxidase is very high in the muscle of this caterpillar. The cytochromes themselves are exceptionally concentrated in the thoracic muscles of adult flies, and it was here that they were first discovered by Keilin. The greater part of the respiratory activity of the developing embryo of *Melanoplus* is attributable to the cytochrome system, since it may readily be inhibited by HCN, CO, or NaN_3, leaving a small residual cyanide-insensitive component. When the embryo is in a state of diapause the total respiration is at a low level, because of the almost total disappearance of the cytochrome component, and is then composed almost entirely of the cyanide-insensitive component.[11] The nature of this latter com-

ponent in insects is unknown, but by analogy with other organisms it may possibly be connected with the cyanide-insensitive "yellow enzyme" of Warburg, which is a flavoprotein catalysing the transfer of H_2 to molecular oxygen from a dinucleotide carrier known as "coenzyme."[5] The oxidase component in these grasshopper embryos requires the cells to be intact; the dehydrogenase component does not.[11]

Carbon monoxide. The combination of carbon monoxide with the cytochrome system has been studied in the pupae of *Drosophila*, where it results in the inhibition of as much as 50% of the oxygen consumption. The degree of inhibition was found to be proportional to the concentration of CO, indicating that the effect was due to a stoichiometric formation of what might be called "carboxy-cytochrome." The inhibition can be partially cancelled by exposure to light, in the same way that carboxyhaemoglobin in mammals may be separated by radiant energy.[228]

Hydrogen cyanide. This toxic gas is deadly to mammals, since it is a respiratory stimulant and thus promotes further intake of the poison. But for insects it is a respiratory depressant and narcotic, and many of the less active species can survive moderate exposure to it. An adult fruit fly placed in HCN vapour will be stupefied within 30 sec, after a fleeting initial excitation. If removed from the vapour immediately after it is narcotized, the fly will recover. But if it is left under cyanide the appendages and wings assume an unnatural position, and recovery becomes less likely.[8] These observations may also be made on adult Lepidoptera in cyanide killing bottles. Certain beetles infesting stored products which have been fumigated for a period of some hours may remain paralysed for several days and then recover.[143]

This initial stupefaction of insects by HCN vapour is associated with a great decrease in respiratory movements.[20] The condition of reduced respiration, described as "protective stupefaction," renders the insect less susceptible to the HCN vapour subsequently applied; this topic has been considered in the previous chapter. The cyanide vapour enters the tissues in a loose combination by a process known as sorption, whence it cannot be removed upon return of the insect to fresh air.[149]

The narcotic effect of the cyanide radical may also be observed in *Periplaneta* injected with sodium or potassium cyanide or potassium ferricyanide.[137] High concentrations induce a rapid narcosis which is soon followed by death. With lower concentrations, the insect may recover from the initial narcosis, only to enter subsequently upon the train of symptoms—excitation, tremors, paralysis—which leads to death (Fig. 3).

Hydrogen cyanide poisons those oxidizing enzymes which contain Fe, such as catalase and cytochrome oxidase.[5,59] The effect of HCN on isolated muscle and fat body of *Carpocapsa* larvae was found to entail a decided inhibition of the oxidative processes which involve consumption of molecular oxygen, accompanied by a stimulation of the glycolytic processes which involve production of CO_2 without consumption of oxygen.[72] Thus the respiratory quotient rises to a figure between 2 and 3. A similar effect was obtained on ground tissue of *Passalus* beetles, where catalase and the phenoloxidases were strongly inhibited, whereas the dehydrogenases were scarcely affected.[188] Experiments on protozoa have shown that HCN is a poison of the cell surface and not of the interior cytoplasm.[31] Oddly enough, HCN was found to completely inhibit the digestive protease of grasshoppers.[186]

Narcotics

This class of compounds demands consideration not because they are themselves insecticides, but because of the importance of a knowledge of the process of narcosis in insect toxicology. Essentially narcosis is a decrease of the activity and irritability of cells and cellular organisms; the effect becomes all the more conspicuous the more active the animal normally is, and thus it is especially noticeable in insects. Although narcosis is often included in the symptoms induced by a contact insecticide or fumigant, it should be remembered that it is not the cause of death. Many narcotics are non-toxic, to the extent that the narcosis is completely reversible, unless the narcotic has been applied in a high concentration or for a long period.

The typical narcotics are the apolar organic compounds which show mutual solubility with lipoids, e.g. ether, the alcohols, acetone, chloroform, benzene, kerosene, and other aliphatic hydro-

carbons. A second group is composed of the so-called narcotic drugs, which include urethane and other carbamates, phenobarbital and other barbiturates, and the cocaine derivatives; these molecules contain little apolar material and their surface activity replaces liposolubility as the narcotizing factor. Finally, certain gases exert a narcotic effect incidental to their main physiological action which is altogether different, e.g. carbon dioxide, hydrogen cyanide, and carbon disulphide.

The symptoms of narcosis as observed in practical control are described by the word "knockdown," denoting paralysis in insects whether reversible or not. The succession of symptoms shown by adult *Musca* under the influence of chloroform or ether vapour has been closely observed. First the legs are simultaneously paralysed, followed by the wings and finally the proboscis and antennae. Recovery of appendages proceeds in the reverse order, from the head to the legs and then the wings; but full muscle tonus is not regained for a considerable time.[90] In the adult *Drosophila* narcotized with ether, the wings and legs are paralysed in the normal position of rest, and recovery occurs in approximately 30 min. These flies may recover without injury from four successive anaesthetizations, each of 2-min period.[147] If they are submitted to ether vapour for a longer period, the wings are folded back, the legs are held stiffly away from the body, and the insect usually dies in that position.[9] A similar picture is shown by *Drosophila* under the initial narcotic action of hydrogen cyanide[8] (see above). Carbon dioxide, however, allows complete recovery even after continuous anaesthesia for more than an hour.[223]

Many compounds show a measure of toxicity when applied to insects at the dosage level required for narcosis. When the housefly is submitted to the vapour of chloretone (trichloro-*tert*-butyl ketone), the paralysis of the appendages is preceded by a period of excitation, ataxia, and spasms. The recovery from narcosis is accompanied by ataxia in addition to the lack of muscle tone, and mortality is frequent.[90]

Most of the volatile organic compounds employed as insect fumigants exert a narcotic effect. When the vapour concentration was set at the median lethal level, most fumigants were found to anaesthetize *Tribolium* within 1 hr, whereas chloroform

exerts this effect within 10 min. High vapour concentrations of most fumigants can narcotize within 2 min. and with chloropicrin the flour beetles may be immobilized in 30 sec.[199] Many fumigants when employed below the lethal concentration have a reversible anaesthetic effect, and some (e.g. *p*-chloroacetophenone for *Tribolium*) are anaesthetic but non-toxic at all concentrations. Vapours of narcotics such as carbon disulphide, diethyl ether, and hydrogen cyanide are without effect on the haemocytes, although the last two compounds have an inhibitory effect on blood coagulation in *Blatta*.[50] However, both carbon tetrachloride and dichloroethyl ether have been found to increase the number of spheroidocytes in *Ephestia* larvae, which develop large vacuoles filled with lipoid.[4a]

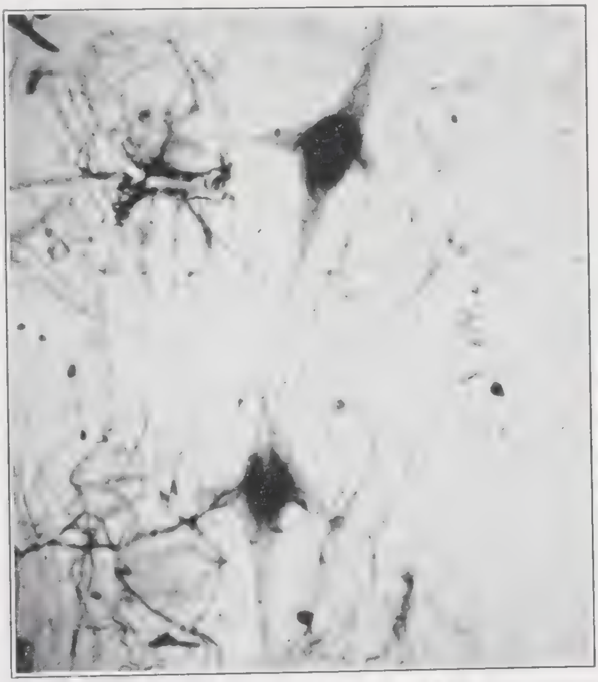


FIG. 7. Uptake of narcotic liquids by ganglia of *Culex* larvae. The penetration of xylol along the fine tracheae into two abdominal ganglia is shown by the dye Sudan B. (From Richards, 1943)

If a narcotic such as xylene is injected into the main tracheae of a *Culex* larva, paralysis follows in 1 min and the heart stops after about 15 min. Tagging the xylene by a Sudan dye (IV or Black B) will reveal that it is taken up by the nerve cord and no

other tissue (Fig. 7). The material is most concentrated in the fibre-tract regions, with which the tracheoles are in connection. Moreover the dye does not enter the axon but is confined to its myelin sheath, which is composed of lipoid, mainly lecithin and cholesterol, bound to protein.[163] The same phenomenon was observed in five other species of insects. When other liquid organic compounds were tested, the most extensive uptake (measured by dye) by the nerve cord was shown by benzene and methylbenzenes, terpenes and pinene, followed by the petroleum hydrocarbons, chloroform, carbon tetrachloride, ethylene dichloride, carbon disulphide, and diethyl ether. All these compounds are narcotics, and the observations showed that they penetrated the nerve cord alone and no other tissue.[168]

If the isolated nerve fibers of an insect are examined under polarized light, they will be found when in health to show birefringence, as a result of the particular orientation of the micelles of the protein and lipoid in them. It may be deduced that the collagenous protein of the axis cylinder—the cytoplasm of the axon—is in the form of micelles oriented longitudinally along its length. The myelin sheath, which is very thin, contains micelles of lipoid and protein oriented radially like spokes on a wheel[164] (Fig. 8). Narcotics such as chloroform, ether, and xylene, when applied to the nerves by injection into the tracheae, were found to destroy the optical properties of the lipoprotein sheath but not of the axis cylinder. However, it must be pointed out that vapours of these narcotics (ether, ethylene dichloride) did not change any of the optical properties, even when in concentrations sufficient to cause death.[165]

It is therefore evident that the typical narcotic vapours exert their effects on insects by preferentially affecting the nervous system. The nervous tissue not only may show a selective uptake of narcotic by virtue of the lipoidal nature of the nerve sheaths, but also may offer a lower threshold for the narcotic effect than other tissues. Insects are susceptible to true anaesthesia in that a reversible effect may be obtained on the action currents of the nerve fibres, and thus on the coordination of the body, without the tissues being adversely affected. This is the condition known as surgical anaesthesia in mammals.[122]

Very low concentrations of a narcotic have an excitatory effect on insects, as they do in mammals, following the Arndt-Schulz "law" that low doses stimulate while higher doses depress. Similarly it is found that the initial stages of narcosis, when the compound has not yet entered the tissues in quantity, are marked by excitation. Grasshoppers anaesthetized with ether showed an initial increase in CO_2 output, followed by a decrease.[10] Finally a constant rate of respiration was established, which may be attributable to an equilibrium concentration of the narcotic being established in the tissues. Very high concentrations or a long exposure period cause cytolysis.[89]

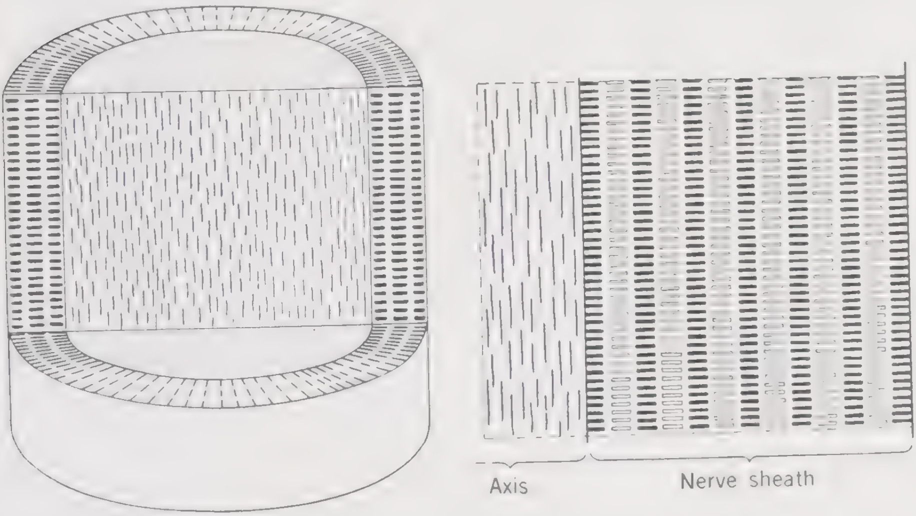


FIG. 8. Orientation of micelles in insect nerve axon and sheath. *Left:* hemisection of nerve, showing longitudinal orientation in axon and radial orientation in sheath. *Right:* enlarged section of sheath, showing lipoid and protein micelles in concentric layers. (From Richards, 1944)

The relative potency of a representative selection of narcotic compounds has been correlated with their relative liposolubility (Overton-Meyer theory). It is generally conceded that the apolar compounds enter the fatty cell membranes and nerve sheaths by a process analogous to the penetration of surface films of cholesterol or phospholipids by the hydrocarbon chains of fatty acids.[179] The relative potency of narcotics has also been correlated with their surface activity, i.e. their ability to reduce surface tension at an interface (Traube theory). It is probable that many nar-

cotics without liposoluble apolar hydrocarbon chains exert their effect on nerve because of their surface activity.[96]

The principal effect of narcotics on the tissue oxidation process is the inhibition of dehydrogenases.[5] They also adversely affect lipases, the higher alcohols exerting an increasing effect as their surface activity increases.[205] The dehydrogenase activity of ground tissues of *Passalus* beetles was reduced by chloroform, carbon tetrachloride, or gasoline, without affecting the oxidases or catalases.[188] Methyl or ethyl alcohol had similar inhibiting effects on dehydrogenase activity in intact larvae of *Musca* or *Tenebrio*.[98]

It was observed by Shafer that the effect of narcotic vapours on the beetle *Passalus* or the grasshopper *Ceuthophilus* closely resembled that caused by lack of oxygen. The succession of symptoms—excitation, ataxia, paralysis—induced by vapours of benzene, chloroform, ether, gasoline, kerosene, hydrogen cyanide, or carbon dioxide, was apparently identical with that obtained in an oxygen-free atmosphere of hydrogen or nitrogen. It was therefore suggested that narcosis of these insects involved tissue anoxia, and particularly the reduction of oxygen supplied to the nerves. Artificial lecithin membranes were found to become less permeable to oxygen when they had been exposed to gasoline vapour. Shafer concluded that in addition to the inhibition of dehydrogenases by the narcotic, the oxidative enzymes were also asphyxiated.[188] It is generally considered that the maintenance of cell membranes and nerve sheaths is dependent on continuous oxidation, and this hypothesis would account for the narcotic action of carbon dioxide and hydrogen cyanide. In mammals it has been found that narcotic drugs depress the oxidation rate of the central nervous system, and that complete anoxia of the brain for 20 sec brings unconsciousness. The inception of narcosis in *Musca* larvae under ethyl alcohol involves an initial decrease in phenoloxidase activity.[98]

When narcosis is no longer reversible and the treated insect is proceeding towards death, a different enzymic picture develops. Larvae of *Tenebrio* or *Musca* about to die from contact applications of chloroform, benzene, hexane, or cyclohexane show an increase in both dehydrogenase and phenoloxidase activity. It is considered that this increase is attributable to the displace-

ment of the protective lipoid from the tissues by the solvent action of the narcotic, thus exposing more enzyme surface. It is suggested that the conversion of narcosis into lethality is due to the accumulation of toxic quinones produced by the increased phenoloxidase activity.[98]

The vapours of narcotics such as chloroform, ether, xylene and ethylene dichloride have been successful in breaking prepupal diapause in *Loxostege*.[148] The vapour of gasoline was found to activate dormant pupae of *Actias luna*. Moreover the developing pupae were found to absorb three times as much vapour as the dormant pupae, indicating possibly that a change in the condition of the tissue lipoids took place when development was resumed.[188] In *Loxostege* the change from prepupa to pupa, whether induced by chemicals or by cold, was preceded by liquefaction of the fat body, and it was suggested that the activation of lipases might be an important factor.[148]

Narcotic drugs. The narcotic drugs exert a more powerful effect on nervous activity than the lipoid solvents considered above, and are thus effective at lower concentrations. Cocaine and novocaine have been employed with success as local anaesthetics for insects, being effective on contact application to particular parts of the body.[183] The local anaesthetic action of procaine has been demonstrated on the crayfish nerve-muscle preparation.[53] A clue as to the mode of action of cocaine has been found in frog nerve and muscle, where cocaine reduces the permeability of these tissues to potassium ions.[189] Its initial effect on the roach, however, is to stimulate the insect.[131]

Atropine also exerts local anaesthetic action in the crayfish nerve-muscle preparation. When injected into *Periplaneta* it renders the insect inactive for a long period, although the roach is still capable of responding to stimuli.[173] Atropine may be employed as a sedative to cure DDT-poisoned insects or to protect them against subsequent DDT poisoning.[131] However, in the larvae of *Automeris*, loss of locomotion due to atropine is accompanied by trembling, increase in irritability, and the symptom described as "reversal of inhibition" in the prolegs.[illegible] The essential action of atropine is considered to be the blocking of the appropriate receptors in nerve so that acetylcholine mediation cannot operate on them.[7]

The barbiturates also exert a sedative antagonism to DDT poisoning in the roach. Adult *Drosophila* narcotized by phenobarbital show a slow recovery accompanied by ataxia. Injection of high concentrations of this depressant drug kills the flies immediately, all appendages falling into the position of normal relaxation.[9]

Urethane has been added to the aquatic medium to anaesthetize ephemerid nymphs, one species out of the six investigated failing to recover from the narcosis; the effect of the drug was to decrease the heartbeat and reduce the metabolism to the basal level.[62] However, injections of urethane or of chloral hydrate had no narcotic effect on *Periplaneta*.[131] The narcotic drugs such as carbamates and veronal were found to inhibit the dehydrogenases of the grasshopper embryo.[27] Urethane and the higher alcohols are known to exert the same effect on mammalian dehydrogenases.[5]

The venom of the solitary Hymenoptera effects a complete locomotory paralysis of their insect victims, but the heart continues to beat. It has been found that the venom of *Sphecius* causes lesions to appear in the ganglia of cicadas they have paralysed.[79] Cobra venom also has a paralytic effect on *Periplaneta* and destroys the ultrastructure of the nerve axon and then of its sheath; lysolecithin, however, is without effect.[165]

Hydrocarbon oils

When an oil such as kerosene is sprayed on the housefly, the struggling insect shortly becomes "knocked down" by a progressive paralysis which passes from the hind legs forward. It usually recovers from this narcosis within 5–15 hr, to resume its career with fertility unimpaired and progeny unaffected.[169] It is reasonable to conclude that the narcosis is a consequence of asphyxiation, and anoxia of the nervous tissue.

Similarly, if kerosene is applied to the surface of water infested with *Culex*, the larvae will become lethargic and sink to the bottom in 10–20 min. Since non-toxic medicinal paraffins and highly refined lube oils are also effective, it is reasonable to conclude that the biological action is due to anoxia. While these larvae are still under narcosis, and before death has set in, their nerve cells are found to show a characteristic clumping of the nuclear

chromatin. The condensed nucleus is surrounded by a halo of clear fluid, and the Nissl granules take on a reticulate arrangement [162] (Fig. 9). Such a condition has been induced by anoxia alone, by depriving larvae of *Sciara*, *Chironomus*, and *Drosophila* of oxygen.[17] It has also been established that chromatin clumping is accompanied by increased nuclear acidity, due possibly to the accumulation of CO_2. The application of a highly refined heavy oil to the scale insect *Phenacoccus* takes 5–15 days to kill, the same amount of time as that involved in asphyxiation by anoxia.[44]

FIG. 9. Suffocating effects of oils on cells of *Culex* larvae. A. From thoracic ganglion. B. From suboesophageal ganglion. Note the clumping of chromatin and reticulation of chromidia. (From Richards, 1941)

In practice most insecticidal oils, such as kerosene and fuel oil, contain olefins, aromatics, and impurities which add a truly toxic effect. The olefins obtained from kerosene kill *Phenacoccus* 3 times as quickly as kerosene does.[44] The kerosene employed in fly sprays from which toxic impurities have not been completely removed by refining causes a certain proportion of the houseflies to die under narcosis. *Passalus* beetles immersed in kerosene are killed in 1 hr, despite the fact that they can live for 38 hr without oxygen.[127] *Culex* larvae may be killed by unrefined kerosene or fuel oil in spite of oxygenation of the water under the oil. In this case death is preceded by convulsions and twitches; and pre-mortem examination of the central nervous system shows degeneration of the fibres and separation of the

inner fibre tracts from the outer cell layer, without the chromatin clumping characteristic of asphyxiation.[162]

That refined saturated oils may be completely non-toxic is confirmed by the entire inability of medicinal paraffin to destroy nerve ultrastructure, which is the first detectable effect of nerve poisons.[165] All oils if applied in high concentration for a sufficiently long period of time cause dissolution of fatty tissue, the gasoline fractions exerting the fastest action.[187]

Naphthalene and paradichlorobenzene

Both these compounds have an effect on isolated arthropod nerve which is similar to that caused by pyrethrins, namely the repetitive discharge of trains of impulses with interlocked spikes[218] (Fig. 13). Naphthalene vapour induces a slow paralysis in insects. The haemolymph reddens or blackens, indicating that the tissue oxidase systems have been disrupted. Post-mortem symptoms are characterized by dissolution of the fat body and other tissues, with the exception of the nerves.[158]

Paradichlorobenzene also is narcotic, increasing the CO_2 output of affected insects until it finally falls before death.[157] In advanced stages of poisoning, paradichlorobenzene dissolves the body lipoids.[212] Its classification as a respiratory poison refers only to its mode of entry as a vapour and not to a specific effect on respiration.[111] When injected into *Periplaneta* it causes tremors and paralysis of a type closely resembling that which accompanies DDT poisoning.[136] Hexachloroethane, another lipoid solvent, is found to exert reversible DDT-like effects on isolated arthropod nerve.[218]

Carbon disulphide

This fumigant compound acts as a narcotic as a consequence of its solubility in lipoids. It is rapidly absorbed into the insect, where it reduces the respiratory rate.[187] Insects fumigated by CS_2 were found to show partial recovery from anaesthesia before they finally succumbed. Cockroaches killed by CS_2 show a great reduction of blood volume.[193] A reduction in cell count has been observed by some authors[illegible] but not by others.[illegible] In advanced stages of poisoning, CS_2 dissolves the body fat.[illegible]

In addition, CS_2 reacts with protein, which it may precipitate.[212] At low dosage levels it inhibits both the oxidases and dehydrogenases, as exemplified by its effect on the luminescence of *Photuris* fireflies, which is not completely reversible.[188] Thus it causes permanent injury in addition to its narcotic effect, and there is evidence that it reacts with the protoplasm of the ganglion cells.[149]

Pyrethrins

The pyrethrins and cinerins derived from the plant *Pyrethrum* are poisonous to all animals, vertebrate and invertebrate, which possess a nervous system. Thus, although they are ineffective against protozoa, they are highly toxic to coelenterates, helminths, molluscs, annelids, and arthropods, and to fish and amphibia. Their toxicity to mammals and birds is very much reduced because of the fact that the high body temperature of these homoiotherms allows enzymic hydrolysis of them to proceed at a sufficient rate to detoxify sublethal doses completely.[29] Thus the threshold dose is raised to the high level of the lethal dose.[65]

If invertebrates such as *Cochylis* caterpillars are raised to mammalian body temperature (37° C), they too can throw off moderate doses of pyrethrins which are normally lethal. Conversely, if a warm-blooded animal such as the dog, which can survive repeated administration of sublethal doses, is given a small fraction of this intake in one single dose (6–8 mg/kg), he will show the characteristic succession of excitation, convulsions and paralysis followed by death from respiratory failure. Thus the susceptibility of insects to pyrethrins, which might at first sight be considered peculiar to them, may be attributed not only to their small size denying them a sufficient barrier to delay the entry of the poison to the vital tissues, but also to the fact that their poikilothermy prevents detoxification from operating fast enough.[29]

The response of insects to poisoning by pyrethrins is characterized successively by (i) excitation, (ii) convulsions, (iii) paralysis, and (iv) death, a sequence typical of nerve poisons. In caterpillars poisoned by a median lethal dosage of pyrethrins these symptoms have been described as follows:[107]

(i) Fast, restless locomotion with dorsum raised, the prolegs strongly prehensile, the head moving from side to side, the mandibles snapping, and food being regurgitated. This stage lasts for less than 5 min.

(ii) Writhing of the whole body, often rolling over and over; head and tail drawn together, then snapped straight, by successive contraction of ventral and then dorsal longitudinal muscles, which may extrude the rectum. This stage lasts for about 4 hr.

(iii) The body becomes motionless and flaccid, and twitches of trunk and appendages become less frequent and ever weaker. Reactions to stimuli gradually disappear. This stage may last up to 5 days.

(iv) The heart may continue to beat weakly and spasmodically for a further period, making the point of death difficult to establish.

The initial excitatory stage may be preceded by a latent period, which is of 1- to 2-min duration in *Bombyx* and *Vanessa*, and 5 min in *Lymantria* and *Stilpnotia*.

The succession of symptoms induced by pyrethrins in the honeybee is (i) restlessness of locomotion and frantic flying; (ii) ataxia, with zigzag flight and locomotion; (iii) progressive paralysis, moving rapidly forward from legs to wings, the bee buzzing on the ground; and (iv) complete paralysis with abdomen curled up, followed by death.[13] The onset of symptoms is hastened the higher the dosage or the more active the insect, leading to the familiar "knockdown" effect observed in adult houseflies. It is considered that the initial excitatory phase is due to stimulation of the peripheral sensory nerves,[36, 100] the convulsions to stimulation of the central nervous system, and the progressive paralysis to the onset of pathological changes in the nervous system.[24]

The initial effect of pyrethrins on *Oryzaephilus*[112] and *Blattella*[56] was found to be accompanied by an abrupt increase in respiratory rate (Fig. 10). Insects recover completely from sublethal doses, provided they have not passed beyond the initial stages of paralysis. Insects that have succeeded in recovering from deeper paralysis may show subsequent necrosis of append-

ages.[201] Adults of *Lasioderma* that had survived pyrethrum sprays were able to deposit only about one-half of the normal number of eggs, presumably because of a permanent incapacitation of their genitalia.[207] Various species of forest defoliators that had survived pyrethrum treatments in the larval stage showed a reduction in the proportion of successful pupations and emergences; this effect was reduced by the intake of food after treatment, and for this reason the more voracious females showed less of this latent effect than the males.[107]

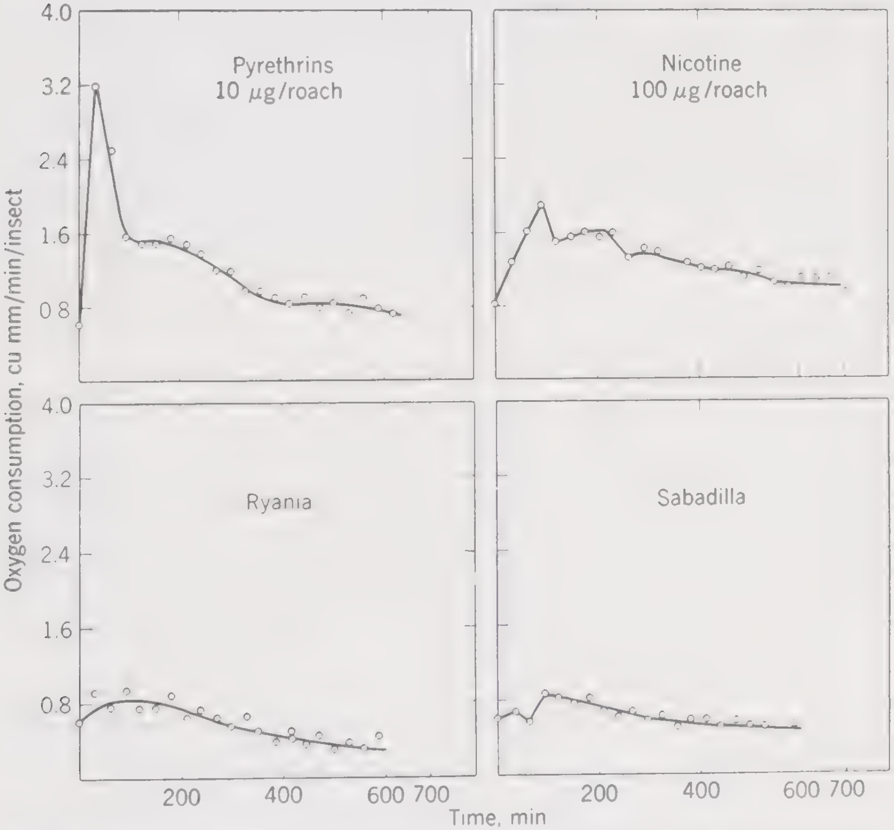


FIG. 10. Rate of oxygen consumption by *Blattella* injected with pyrethrins, nicotine, ryania, or sabadilla. (From Harvey and Brown)

Smaller doses will lead only to the convulsion state, and even smaller merely to excitation; the dose for convulsions is one ten-thousandth of the fatal dose of 250 mg/kg for *Galleria* larvae by injection.[9] The latent period, i.e. the time to reach the excita-

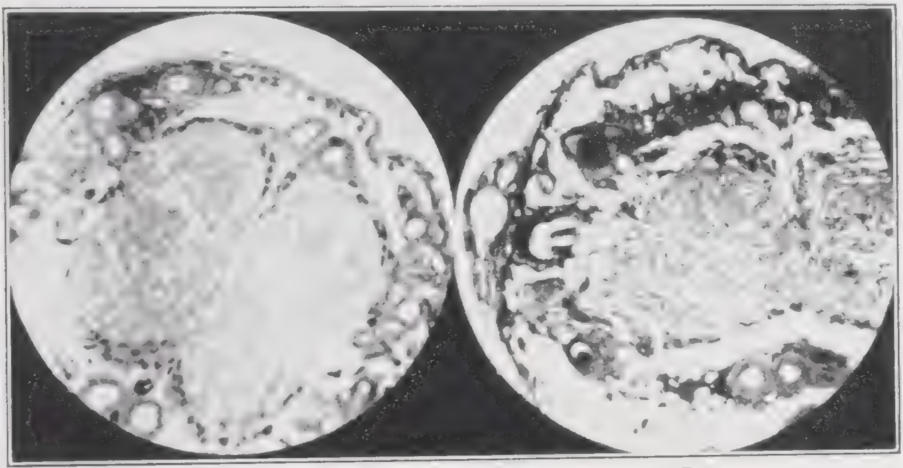
tory phase, is a function of the concentration of pyrethrins, where the reciprocal of the period is logarithmically proportional to the concentration.[172] The same relationship applies to stoppage of the heart of *Galleria* by perfused pyrethrins. In the intact insect, pyrethrins in sublethal doses initially stimulate the rate of heartbeat, but depress it at higher doses; they exert a similar effect on the rate of blood circulation, which ceases before the heart stops beating.[35] The effect of pyrethrins on the insect heart is reversible right up to the time when stoppage becomes permanent.[6] Stoppage of the isolated heart of *Blatta* was found to occur typically in systole,[232] and of *Galleria* in diastole.

Pyrethrin I is much more toxic to insects than pyrethrin II, whereas with vertebrates the reverse is evidently the case. The powers of detoxification exhibited by *Pieris* caterpillars in the alimentary canal are sufficiently rapid to render pyrethrins non-toxic as stomach insecticides, although by contact they are highly toxic to this species.[202] In larvae of *Prodenia eridania*, the alimentary canal and muscles show moderate powers of detoxification, while the fat body is very effective and the blood quite inert in this respect.[226]

Uncertainty exists as to the toxicity of pyrethrin vapour. The vapours from pyrethrum powder have been found to be toxic and irritating to *Hippodamia*[155] and to be a poison and respiratory stimulant to *Passalus*.[187] Yet air bubbled through pyrethrum extract or confined over powder was found to be non-toxic to *Apis*.[67] Recent work has shown that the vapour from concentrates of high pyrethrin I content is very slightly toxic and repellent to adult *Aedes* mosquitoes.[30]

Pharmacologically the pyrethrins closely resemble veratrin in their effect on mammals[29] and on isolated arthropod nerve-muscle preparations.[53] Their application to the isolated nerve cord of *Blatta* first excites a massive discharge of many types of nerve impulse, followed by repeated synchronized discharge of continuous trains; eventually the response to stimulation falls and finally fails altogether.[120] In living insects poisoned by pyrethrins the nerve conductivity was found to be decreased to about one-fifth of the normal.[107] It is considered that the pyrethrins enter the nerve sheath as a consequence of their lipoid affinity, and that they spread through the body by way of the

nerves[107] and more particularly their outer sheaths.[99] Thus it is found that section of the nerve cord at the junction of thorax and abdomen has the effect of preventing the spread of symptoms forward from the abdomen.[100]

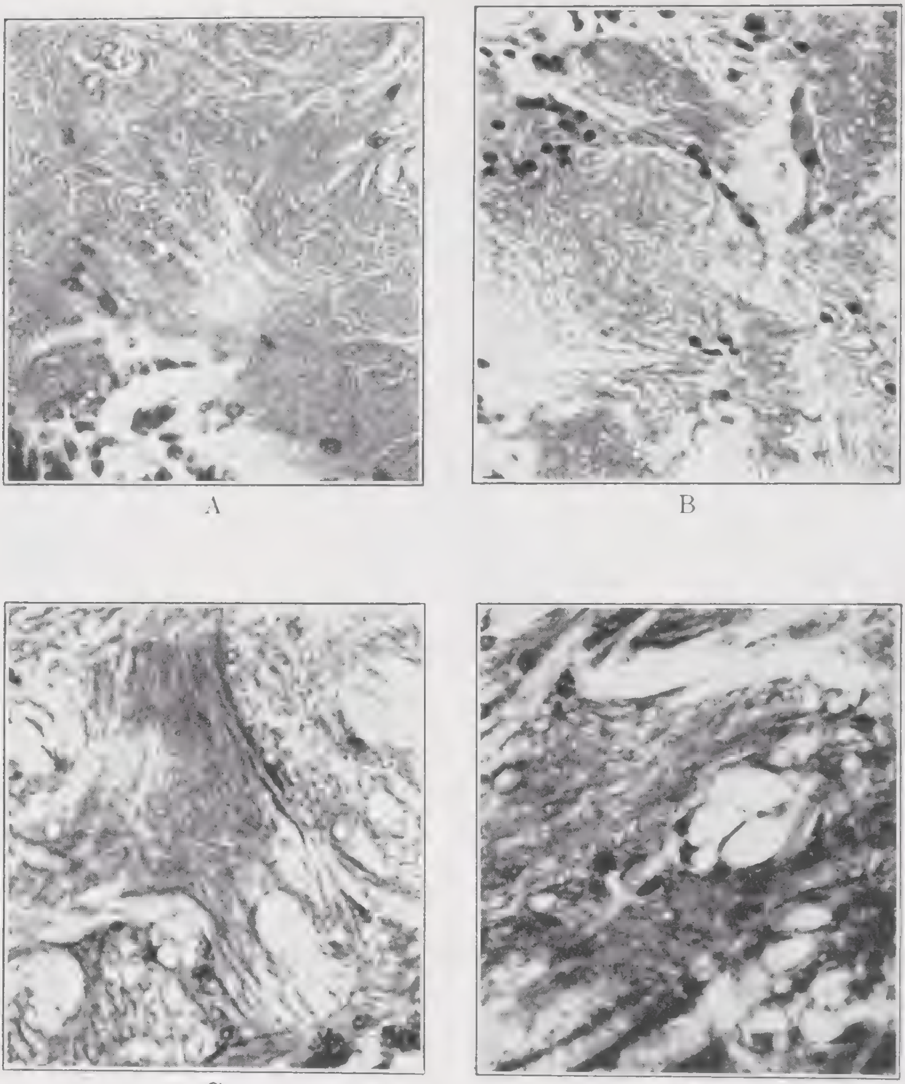


A B

FIG. 11. Histopathology of pyrethrum in *Lymantria* larvae. Sections of abdominal ganglia of (A) untreated larva, and (B) larva treated with pyrethrum extract. Note the cell destruction. (From Klinger)

The first visible change to occur in the nervous tissue of *Periplaneta* poisoned by pyrethrins is a decay of the birefringence normally shown by the protein of the nerve fibre, accompanied by clumping of nuclear chromatin in the nerve cells.[165] Then the birefringence of the lipoid myelin sheath starts to decay, vacuoles appear in the nerve cells, and the nuclear chromatin shows dissolution. Finally, when the nerve ultrastructure, as indicated by the birefringence, has entirely disintegrated and the insect is in the early stages of paralysis, the typical pyrethrin lesions of the ventral nerve cord and brain appear (Figs. 11 and 12).

These lesions are characteristic of pyrethrin poisoning to the extent that they are not shown in acute cases of nicotine or lead arsenate poisoning,[222] or by rotenone unless applied in the very high concentrations sufficient to give a knockdown effect.[50] As studied in *Melanoplus*, *Tenebrio*, *Lymantria*, *Musca*, *Rhodnius*,[220] *Corethra*, and many other species, they appear mainly in the



A B C D

FIG. 12. Histopathology of pyrethrum and sesame oil in brain of *Musca* adults. Sections through brain of housefly in region of corpus centrale and fibre tracts laterad of it, fixed in formalin and stained with haematoxylin and eosin-y (×500). A. Normal check. B. Effect of pyrethrum: dissolution of fibre tracts and presence of clear spaces. C. Effect of sesame oil: vacuolation of nerve cells. D. Effect of sesame oil and pyrethrum: vacuolation and lysis of tissue. (From Hartzell, 1945)

segmental ganglia, in the brain, and to a less degree in the connectives. A general indication of histological damage is afforded by the cells taking on a violet colour when stained with toluidine blue.[222] Vacuoles may appear in the cytoplasm of the nerve cells.[78, 81, 110] The tigroid (reserve food material) of the Nissl granules may be dissolved.[80] Owing to the dissolving of the lipoid sheaths, many nerve fibres show lysis, and clear empty spaces appear in the fibre tracts. The nuclear chromatin of the nerve cells becomes compacted into clumps, an effect presumably attributable to local tissue anoxia due to the presence of the narcotic pyrethrins in the lipoid sheaths.[80, 165]

Other tissues are affected by pyrethrins, though to a less degree. In the aquatic larva *Corethra*, vacuoles appear in the muscle cells within 15 min of exposure, and in 24 hr even the hypodermal cells show vacuolization and are loosened from the cuticle.[110] Examination of the head muscles of houseflies in the process of being killed by pyrethrins revealed separation of the fibrils (fenestration) and loss of striation, while the nuclear chromatin was compacted into dense rods (Fig. 13). However, intravital staining in a number of insect species failed to show any histological change in muscle tissue after pyrethrin poisoning.[107]

It is still a moot point whether pyrethrins may be considered as neuromuscular poisons[102] or as purely nerve poisons.[184] According to the latter view, the loss of muscle tone is a consequence of the primary nerve effect,[107] and histological changes where they occur in muscle are secondary. The former view is reinforced by the evidence that in crickets (*Gryllus*) poisoned by pyrethrins the chronaxie of muscle is raised from 1 to 4, while the nerve chronaxie remains unchanged; and that stomach muscle isolated from nerve will lose tonus and suffer paralysis on treatment with pyrethrins.[171] The two views may be reconciled by the consideration that pyrethrins resemble narcotics in affecting all tissues, and that the threshold for nerve is lower than for muscle or other tissues.

Synergists. It has been found that certain compounds, when added to pyrethrum fly sprays, so increase toxicity that the dose of pyrethrins sufficient to induce knockdown may be reduced a hundredfold. The first to be discovered, namely the sesamin

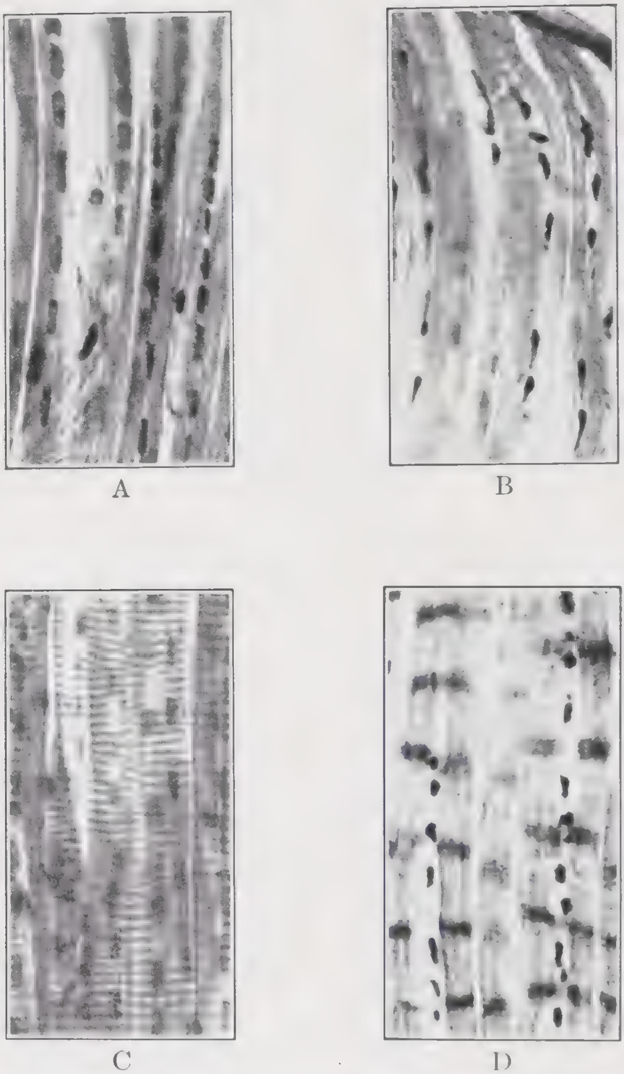


Fig. 13. Histopathology of pyrethrum and sesame oil in muscle of *Musca* adults. A. Normal check. B. Pyrethrum: nuclear clumping into dense rods. C. Sesame oil: nodes and Krause's membrane greatly accentuated. D. Sesame oil and pyrethrum: clumped nuclei and prominent bands. ×500. (From Hartzell, 1945)

present in sesame oil,[40] was followed by other methylenedioxyphenyl compounds such as piperine, fagaramide, the N-substituted piperonyl amides, propyl isome,[82, 83] piperonyl cyclonene, and piperonyl butoxide.[215] Certain terpene derivatives such as *Thanite*, DHS activator, terpin diacetate, and pine oil have increased the toxicity of pyrethrum in fly sprays.[151, 152] A synergist was also found in N-isobutylundecylenamide (IN930), developed for pyrethrum as a lousicide;[18] N-substituted derivatives of methylvaleramide and cyclohexoxyacetamide have also been found effective.[117] There are also cases of pseudo-synergism, as in the effect of lubricating oils, oleic acid, and the "oiliness" of IN930, sesame oil, and pine oil in stabilizing the droplet size of pyrethrum aerosols to ensure contact and persistence on the insects' bodies;[12] and as in certain antioxidants such as pyrogallol and isopropylcresol.

The essence of synergism is that pyrethrum plus adjuvant is highly toxic where each material separately is without effect, the toxicity of the ensemble being greater than the sum of its parts. It has been found that if the adjuvant is sprayed before the pyrethrum, the synergistic effect is just as strong;[13, 118] sesamin applied 24 hr before the pyrethrins allows the same percentage knockdown of *Musca* as when the materials are sprayed together. But there is no synergism if the adjuvant is applied after the pyrethrum, although there is some effect if applied within an interval less than 30 sec.[118] If the insect is pretreated by topical application of the adjuvant to one part of the body, the synergistic effect on knockdown is shown even when the pyrethrins are later applied to another part of the insect's body.[224] All the most important synergists exhibit this property.[229a]

Evidently the synergist, be it an amide, a piperonyl, or other methylenedioxyphenyl compound, effects an alteration in the insect so as to predispose it to pyrethrum poisoning. The synergist has rendered the insect incapable of recovering from the narcotic effect of the pyrethrins. It has been established that DHS activator causes lysis of the non-fibrous cellular components of the housefly's brain, IN930 causes chromatolysis of the cell nuclei,[81] and sesamin induces vacuolization of the larger nerve cells.[83] Piperine induces both lysis and vacuolization, besides destroying the fibre tracts.[82] Incidentally, these synergists

effect changes in muscle also, to accentuate the appearance of the nodes and Krause's membrane.[80, 82] It has therefore been suggested that the synergists operate by so damaging the nerve cells that they can no longer repair the injury which the pyrethrins inflict on the nerve fibres.[224] From a biochemical standpoint, it is equally possible that the synergist may poison the enzymes responsible for the hydrolytic detoxification of the pyrethrins.

It has been found that DHS activator exhibits synergism with rotenone against *Musca*, and that piperonyl cyclonene and butoxide are synergistic with low concentrations of rotenone against *Epilachna*.[17] Another compound that has shown synergism with rotenone is chlordane, which has exhibited slight synergism against *Epilachna* and *Aphis fabae*.[200] A number of materials have been found to be activators of nicotine, but since this is due to their alkalinity liberating the more toxic alkaloid from its salt, it is not a case of true synergism. However, potassium salts were found to have a synergistic effect on the paralytic action of nicotine on *Periplaneta*, whereas sodium salts had little effect.[114] Diphenyl sulphide and phthalonitrile have proved to be real synergists for nicotine,[3] while pentachloroanisole is not; phthalonitrile is not synergistic for all species tested.[121a] Piperonyl cyclonene and *n*-propyl isome have been found to be activators for ryania dust.[161a] The pyrethrum synergists have not proved to be adjuvants for DDT.[43]

Nicotine

Nicotine is a fast and decisive poison for insects and is an excellent contact insecticide. Penetration into the insect is aided by the ability of nicotine to volatilize and enter the tracheae as a vapour. It is also a powerful stomach poison while it still remains on the food; this period may be extended by the use of nicotine bentonite or other forms of fixed nicotine.

In common with other insect nerve poisons, nicotine applied by contact may cause the characteristic sequence of excitation, convulsions, paralysis, and death; and it has a similar action on higher animals. The onset of these symptoms is roughly 10 times as fast with nicotine as with pyrethrins.[141] The initial excitatory phase may increase the metabolic rate by as much as 200 times.

as occurs in moths, which respond to nicotine by violent vibration of the wings.[161] Caterpillars show violent convulsions, with regurgitation, before the onset of paralysis.[74] If, however, nicotine is injected into *Bombyx*, *Celerio*, or *Carpocapsa* larvae, the convulsions do not precede paralysis.[91, 126]

When applied as a covering spray to aphids, nicotine will kill them in 30 min. They are first temporarily narcotized *in situ* on the leaf, and then withdraw the proboscis and show ataxia of the legs. Paralysis follows, progressing forward from the hind legs to the antennae, and the aphid falls from the leaf. The paralysed insect shows twitching of the extremities until death, when the legs curl up; by this time the cuticle is perfectly dry. The honeybee orally poisoned by nicotine also shows locomotory ataxia followed by paralysis spreading forward to the head, followed again by twitching of the appendages and spasms of the abdomen. However, a period of inactivity and dulling of the senses precedes the paralytic symptoms; and, provided the stage of locomotory ataxia is not reached, the bee survives.[125] When injected into *Blattella*, nicotine causes a rapid rise in the respiratory rate, which then gradually falls as the insect lies paralysed[56] (Fig. 10).

If nicotine is applied to the dorsal surface of the cervical region of *Periplaneta*, the insect swallows air and the body swells.[35, 141] If it is applied in vapour form to *Nyctobora*, nicotine first induces spiracular closure, and later destroys the ability of this cockroach to control its spiracular movements.[106] While the insect is showing convulsions, the rate of heartbeat is doubled; it then decreases, undergoing periodic stoppages as paralysis sets in, and occasionally reversing its directional sequence; in some cases the heart stops completely some time before death.[35, 141] When perfused past the isolated heart of *Blatta*, low doses of nicotine increase the amplitude and rate of beat, whereas high concentrations arrest the heart completely.[230] Similarly applied to *Melanoplus*, low concentrations cause a temporary increase in heartbeat, high concentrations decrease it, and very high concentrations stop it; the heart paralysis is, however, reversible.[79] Stoppage of the isolated heart occurred in diastole in *Prodenia*, as contrasted with systolic stoppage in *Blatta*.[230]

It is concluded that in arthropods, as in other animals, the site of action of nicotine resides in the "synapses" between nerve fibres which are particularly located in the ganglia. Nicotine has been found to block synaptic transmission in the isolated nerve preparation of the crayfish *Cambarus*.[219] Application of nicotine to the ganglion of an isolated leg reflex arc of *Periplaneta* results in violent tremors of the leg, which disappear on severing the leg from its connection with the ganglion. Injection of nicotine into the leg alone has no effect, showing that nicotine does not act on the nerve fibres, but only on the ganglion. When applied to the brain of a roach whose haemolymph has been immobilized by cauterization of the heart, nicotine causes tremors to appear throughout the body, which cease upon decapitation. Thus the effects of nicotine, which acts on the telephone exchange, as it were, can mask the symptoms of DDT, which acts somewhere along the lines or at the peripheral ends.[233] However, nicotine does exert a transitory effect on the nerve axon of arthropods, causing repetitive discharge much as the pyrethrins do. Low doses increase the action currents in the isolated insect nerve cord, and really high concentrations are required to block the currents, an effect which is reversible on removing the poison.[179]

When an arthropod nerve-ganglion preparation has recovered from an application of nicotine, it is found that its synapses are rendered immune to further blockage by a second application.* It is as if the appropriate receptors for the drug were still occupied by the molecules of the first application, which have been detoxified, so that the second application cannot reach the receptors to produce synaptic block. Anabasine and nornicotine also can protect the ganglia against a subsequent application of nicotine, as if they too were held on the same receptors and there reduced to innocuousness. On the other hand, the anticholinesterases DFP and eserine, which both block synaptic transmission, do not exert this protective effect, presumably because they do not act upon the same receptors as nicotine.[219]

In most of the insects that have been studied, with the exception of *Drosophila* larvae, *l*-nicotine is more toxic than its *d*

* This phenomenon may be connected with the tolerance of tobacco insects to nicotine; e.g. that of *Protoparce 15-maculata* (G. Beall. 1941. *72nd Ann. Rep. Ent. Soc. Ont.* pp. 24–25).

isomer. From examination of animals from the most primitive phyla up to mammals, it has been found that all species showing higher susceptibility to the *l* isomer exhibit the acetylcholine system for transmission of nerve impulses.[66]

In contrast to the rather definite pharmacological verdict obtained for nicotine, it is not known whether this poison exerts any specific effect on the enzymes of nervous tissue. It proved neither to inhibit nor to stimulate the dehydrogenases or catalase of ground tissues of *Passalus*.[188] However, if added to a suspension of the fat cells and oenocytes of the honeybee, nicotine was found to give cellular effects analogous to those of anoxia in unicellular animals. The cytoplasmic globules of the fat cells become granular, the refractive bodies of the oenocytes disappear, and finally the cell walls of both types of cell disintegrate.[125] Similar disintegration is induced by nicotine on protozoans and coelenterates.[73] For this reason the suggestion has been made that nicotine interferes in some way with the oxidation-reduction system of the cell.

Anabasine

The toxicological effects of anabasine closely resemble those of nicotine, to which it is similar in molecular structure. Like nicotine, it blocks synaptic transmission, but much higher concentrations are required to do so. Preliminary treatment with anabasine will proof the ganglion against subsequent application of nicotine, indicating that the same tissue receptors are involved.[219] It is the equal of nicotine as a contact poison to aphids, but is its inferior in stomach toxicity to silkworms and grasshoppers. Anabasine also exercises a degree of fumigant toxicity.

Its contact action on *Scirtothrips* was found to involve ataxia and convulsions, followed in 10 min by a paralysis that was complete except for slight movement of extremities, which might continue for 2 days before death.[124] Larvae of *Pteronus* (*Nematus*) temporarily immersed in anabasine solutions underwent paralysis from which they could recover. *Pieris* larvae similarly treated became sluggish, and death commonly occurred at the subsequent moult. The respiratory rate in *Pteronus* never de-

creased below the normal even during paralysis, but in *Pieris* it decreased gradually until death.[182]

The contact application of anabasine to *Pteronus* larvae increased its heartbeat to as much as 4 times the normal rate; the increase was less if the nerve cord was severed. If applied directly to the exposed heart, even very dilute solutions of anabasine caused immediate stoppage. Anabasine readily penetrates cuticle that has been cleaned of hypodermis, and increases its subsequent permeability to aqueous liquids. The suggestion has been made that the contact action of anabasine involves a narcosis of the hypodermal cells.[182]

Rotenone

The toxic compounds of *Derris* and *Lonchocarpus* roots, known as the fish poisons, consist mainly of rotenone, deguelin, tephrosin, and toxicarol. Rotenone accounts for approximately one-half the toxicity of these plant preparations to insects.

The poisoning of insects by rotenone is characteristically a slow process, and death may draw on without a struggle. The sequence of toxic symptoms appearing in larvae of *Bombyx*, *Vanessa* or *Dendrolimus* on contact application of rotenone may be characterized as follows: [107]

(i) First 2 days: Inactivity and refusal to eat, occasional regurgitation, locomotion on stimulation.

(ii) 2–6 days: The larvae rest on their sides and slowly bend and unbend the body.

(iii) 6–8 days: Paralysis involving complete relaxation of all muscles of the body.

(iv) The body shrivels, the blood darkens, and the cuticle dries, but the heart continues beating slowly.

Death may be so gradual that peripheral parts may start to decay before the dorsal vessel has stopped beating.[24] In the honeybee, however, the gradual paralysis is preceded by a pronounced restlessness similar to that caused by pyrethrins.[14]

Insects poisoned by rotenone, such as caterpillars and cockroaches, show a drop of some 50% in the rate of oxygen consumption [208] (Fig. 14). This may be a result of depressed mechanical respiration, since derris dusts have been found to stop

the movements of the tracheal opercula of *Bombyx* and *Heliothis* larvae. The depression of air intake in turn may decrease the rate of heartbeat. When derris is applied as a dust to *Bombyx*, there is first a latent period of 40 min during which no outward sign of poisoning is evident, but towards the end of the period the heartbeat drops slightly from the normal rate of 70 per minute (Fig. 14). Then there follows a 10-min period when the caterpillars are highly active and the heart rate shows irregularity, short bursts of stimulation alternating with occasional stoppage; and a further 10-min stage of ataxia during which the heart rate falls to 20 beats per minute, a level which is maintained during the subsequent long paralytic period in which the larvae lie quiescent on their sides.[208] A similar depression of respiration on application of rotenone has been observed with *Oryzaephilus*[119] and *Blattella*.[86] The continuous depression of the rate of heartbeat has also been observed in *Periplaneta*[112] (Fig. 2).

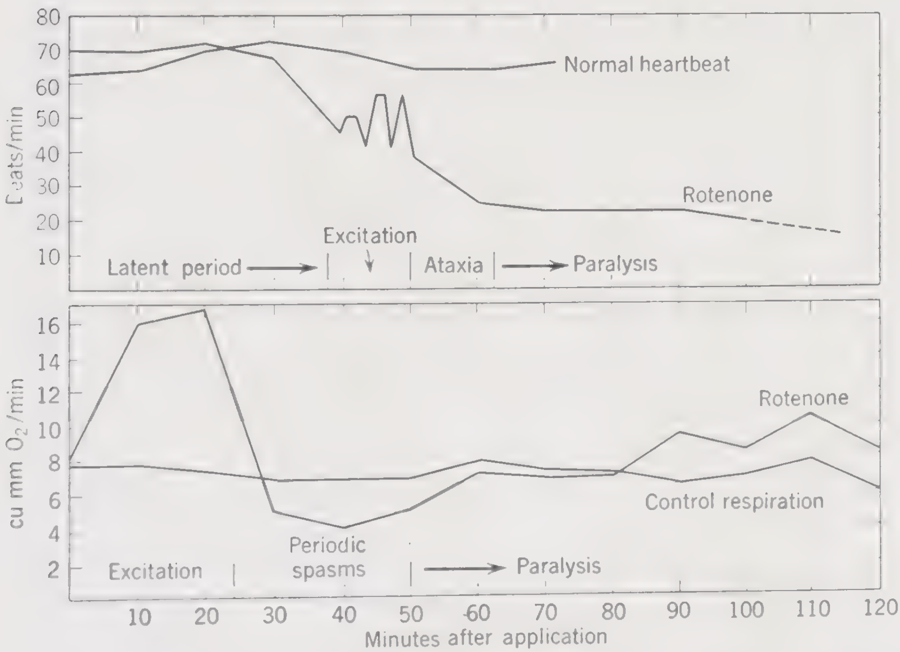


FIG. 14. Effect of rotenone on heartbeat and respiration. *Upper graph: Bombyx* larvae dusted with derris powder. (From Tischler) *Lower graph: Blattella* adults sprayed with cube extract. (From Harvey and Brown) Symptomatic stages indicated on time scale.

Preparations containing rotenone have been employed as contact insecticides as well as stomach poisons, but they have no fumigant effect.[127] The contact action is conspicuous in soft-bodied insects such as aphids, mosquito larvae, and the sheep ked *Melophagus*. It is considered probable that derris dust is dissolved in the body exudations and carried across the intersegmental membranes. However, rotenone appears to encounter more difficulty in penetrating the insect cuticle than nicotine or the pyrethrins.[91] It is unable to poison by contact those species of sclerotized beetles which are highly susceptible to applications of pyrethrins.[149] Grasshoppers and certain species of cutworms which are resistant to contact poisoning by rotenone have been found to be highly susceptible to injection of the poison, showing that cuticle impermeability is the factor causing this resistance.[208]

Rotenone acts as an effective stomach insecticide for caterpillars and the potato beetle. However, it has been found to pass through the alimentary canal of *Prodenia* larvae almost completely undigested and unabsorbed. Indeed, the faeces of these caterpillars contain almost as much of the toxic principle as the food; and no rotenone may be found in the tissues, although they lack the enzymic power to decompose it.[225] It has been suggested that the oral toxicity of rotenone to silkworms is due not to its absorption across the gut wall, but to its paralytic effect on the mouth-parts, which results in an inhibition of further feeding and a slow death by starvation.[64]

That rotenone is a paralytic nerve poison is more apparent in the vertebrates, where it is considered to impair the normal function of the medulla oblongata.[26] It is a fish poison *par excellence*, exerting its main effect through the gills. Its pharmacological action in simpler animals is more obscure. It has shown no effect on isolated crayfish nerve[53] or on the histological picture of nerve or muscle.[107] Only when applied in unusually high concentrations sufficient to cause knockdown in houseflies will it induce the characteristic brain lesions of fibrolysis and vacuolization.[50] In *Thermobia domestica*, sublethal doses of rotenone have been found to cause a latent injury consisting of necrosis of appendages, which may be checked or lost at moults, or may continue until death.[201] In lepidopterous larvae, rotenone poisoning

causes considerable mortality to occur during the moulting process.[107]

The effect of derris on unicellular animals such as the amoeba is to destroy their characteristic shape and disintegrate the cell wall, in a way similar to anoxia under nitrogen. The symptoms induced by derris in the crustacean *Cyclops*, particularly the retardation of the rhythmical intestinal movements, have also been compared to the results of anoxia. Thus it is suggested that the rotenone poisons derive their effect from depressing tissue oxidation. In the insects the tissues are also deprived of oxygen because of the cessation of mechanical respiration, which in turn is caused by the depressant action of rotenone on nerve and muscle concerned in tracheal ventilation.[208]

Other plant poisons

Quassiin, the rotenoid principle of the quassia shrub, resembles rotenone in that it kills insects slowly, and the victim passes without convulsions into a protracted flaccid paralysis. Veratrin or protoveratrin, the toxic principle of "hellebore," closely resembles the pyrethrins in its pharmacological action. When injected into *Melanoplus*, it was found to cause initially a general excitation.[29] Like pyrethrins, veratrin induces in isolated crayfish nerve a tendency to repeated discharge and a lengthening of the refractory or rest period.[58] Its effect on vertebrates is also similar to that of pyrethrins in causing paralysis of nerve centres.[29] The addition of veratrin to crushed tissues of *Passalus* was found to inhibit slightly the dehydrogenase activity.

Veratrin alkaloids are also employed insecticidally in the form of sabadilla seeds, of which the most important constituent is cevadin. The gross symptoms veratrin alkaloids induce in insects suggest that the nervous system is involved in their action. However, adult *Blattella* injected with sabadilla extract,[56] and adult *Oncopeltus* treated with sabadilla by contact,[32] showed only a slight increase in the rate of oxygen consumption (Fig. 10). Tissues of the poisoned milkweed bugs showed a significantly increased activity in the cytochrome oxidase and succinic dehydrogenase systems, but not in the malic dehydrogenase system.[32]

Recent work on ryanodine, one of the most active principles of *Ryania* extract, indicates that it is an unusual insecticide in that its specific site of action is striated muscle. It interferes with the contractile process so as to produce flaccid paralysis in *Periplaneta* and *Bombyx*. During this paralysis the insect does not respond to mechanical or chemical stimuli, but its oxygen consumption averages twice the normal rate.[57] A slight rise in respiratory activity was also noted in *Blattella* injected with ryania extract [56] (Fig. 10). On the other hand, this poison appears to have little or no action on the excitability and conduction of cockroach nerve. Since commencing or partial paralysis in the roach, as in the frog, is quite tremorless, it appears that ryanodine interferes either with the respiratory enzymes or with the phosphagen-adenosinetriphosphate-actomyosin system of striated muscle.[52]

Thiocyanates

The thiocyanates resemble pyrethrins in causing rapid knockdown and paralysis of active insects.[81] However, they do not induce the initial violent stimulatory effect characteristic of pyrethrins; this was found to be lacking on application of butoxythiocyanodiethyl ether (*Lethane 384*) to *Blatta*.[100] Contact poisoning of *Periplaneta* by thiocyanopropyl phenyl ether involves longitudinal body twitches and progressive paralysis passing forward from the hind legs.[55] Application of the median lethal dose of thiocyanoethyl laurate (*Lethane 60*) to *Blattella* causes a brief period of excitement, followed by extension of the appendages and twitches of the extremities, before the final onset of complete paralysis. The initial symptoms are accompanied by a considerable decrease in oxygen consumption, the rate over the whole period of poisoning being roughly one-half the normal respiration.[56] A similar decrease has been observed in *Oryzaephilus* poisoned by *Lethane B71* applied by contact.[119]

Contact application of *Lethane 384* to *Periplaneta* results in an immediate decrease in the rate of heartbeat and blood circulation. If the dose is sublethal, heartbeat [142] (Fig. 10) and circulation will show a subsequent rise. These symptoms resemble those caused by hydrogen cyanide so closely that it has been suggested that the thiocyanates also are respiratory poisons, act-

ing particularly on the respiratory and circulatory muscles.[35] However, although animal tissue is capable of liberating hydrogen cyanide from the simpler thiocyanates, it is unable to release this poison from the higher thiocyanates which show much greater contact toxicity.[168] The thiocyanate insecticides have been found to exert a gradual depressant effect on a heart preparation of *Blatta* in which the segmental nerves have been severed. The heart finally stops in diastole, the alary muscles failing to relax from a contracted position.[232]

The histological effect of *Lethane 384* applied to adult houseflies has been found to involve destruction of nuclear membranes in muscle and disintegration of the non-fibrous cells of the brain.[80] The isobornyl and fenchyl thiocyanoacetates contained in the preparation *Thanite* cause vacuolization of the nerve cord of *Culex* larvae [165] and of the larger nerve cells of *Musca* adults.[80] Thiocyanopropyl phenyl ether induces the appearance of vacuolization, tigrolysis, and cellular degeneration in the abdominal ganglia of *Tenebrio* larvae.[85]

The effect of thiocyanates on insects is different from that on mammals, where they act as paralytics rather than narcotics of the central nervous system, the simpler thiocyanates showing the highest activity.[206] In insects the narcotic effect appears to be predominant, the main effect of the —SCN group being to inhibit cellular metabolism.[212] The thiocyanates tested (*Lethane 384* and *Thanite*) were found to be without effect upon the cholinesterase of insect nerve.[166]

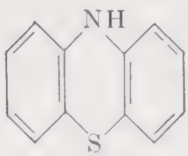
Phenothiazine

This material has given very erratic results when used as an insecticide. Whereas it has proved highly toxic to dipterous larvae when mixed in the food medium (*Cochliomyia*, *Phormia*, *Lucilia*) or the aquatic medium (*Chaoborus*, *Culex*), it has on occasion been entirely ineffective against caterpillars, grasshoppers, cockroaches, bees, and beetles.

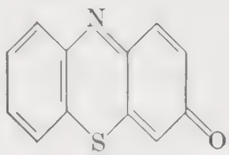
Phenothiazine shows stomach toxicity to *Prodenia* larvae, in which mortal symptoms set in slowly and quietly, without histological lesions appearing.[227] But no stomach toxicity is shown to the roach *Periplaneta*, since phenothiazine is not absorbed

into the haemolymph in any form; it is slowly converted in the mid-gut into leucothionol, which is passed into the hind-gut.[236]

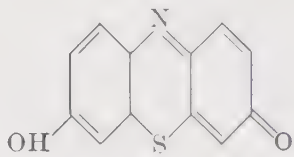
Contact poisoning by phenothiazine is initially marked in the cockroach by locomotory ataxia. The insecticide enters the haemolymph after being oxidised into a conjugate of leucothionol, which is considered to be the active poison. This material is removed by the Malpighian tubules, which also may oxidize part of it. If the contact dose of phenothiazine is of short duration, or if it is in the form of large particles, the insect may recover from the initial symptoms, presumably because of the leucothionol conjugate being excreted concurrently as it is produced.[236]



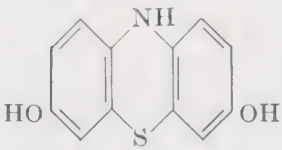
Phenothiazine



Phenothiazone



Thionol



Leucothionol

The effect of phenothiazine is a typical flaccid paralysis, and the course of respiration in the poisoned cockroach resembles that of rotenone. In the gnat *Chaoborus*, the heart of the paralysed larvae may continued to beat for as long as 3 weeks, and recovery may occur after as much as 4 days of immobility.[45] When injected into *Blattella*, phenothiazine has no effect on the respiratory activity except to reduce it slightly, even when the insect is in paralysis.[86]

The ketone phenothiazone similarly shows contact toxicity but not stomach toxicity to the cockroach. The further oxidised compound thionol is neither orally toxic nor by contact. It forms an oxidation-reduction system with leucothionol which is considered to be the toxic principle.[236] Phenothiazine or its derivatives are inhibitors of cytochrome oxidase and succinic dehydrogenase in mammals.[31] This is probably more closely related to its mode of action than the fact that it strongly reduces

synaptic transmission in the crab,[34] and that its intermediaries may inhibit serum cholinesterase.[33]

Thiourea

This compound has been found to be, like phenothiazine, highly toxic to dipterous larvae. It has been suggested that its effect on *Lucilia* may be associated with an upset of the protein metabolism which is so important in these larvae.[95] Of many chemicals tested, only thiourea and potassium thiocyanate were capable of breaking the pupal diapause of *Rhagoletis completa*.[14]

Thiourea induces hyperplasia of the thyroid of mammals[101] and inhibits the metamorphosis of amphibia.[101] Its α-naphthyl derivative, ANTU, is a powerful and specific rodent poison. Susceptibility to thiourea derivatives (e.g. the taste of phenylthiourea) varies greatly according to the genetical constitution of the animals tested. Similarly the different strains of *Drosophila* have been found to show great variation in the susceptibility of their larvae to thiourea.[70]

Miscellaneous nerve poisons

Valone (2-isovaleryl-1,3-indandione) is an excellent acaricide and lousicide, but it is almost without effect on the roach *Periplaneta* when administered orally or applied by contact. If, however, it is injected into the tracheae of the haemolymph, it causes immediate paralysis, from which there is no recovery. All transmission of nervous impulses is blocked; this is not a result of the accumulation of acetylcholine, since valone is not an inhibitor of the insect cholinesterase.[166] The poison is found to destroy the ultrastructure of the protein micelles in the nerve axon, but the birefringence of the lipoid nerve sheath remains unaffected. No tissue pathology can be detected except a moderate degree of clumping of the nuclear chromatin. Similar effects are obtained with 2-pivalyl-1,3-indandione, also called *tert*-butyl valone.[165]

2-Ethylhexanol ("octyl alcohol") is a general poison; in addition to affecting muscle fibres, it induces cytolysis of the insect nerve cord, which becomes opaque and shrinks. Similar pathological changes are caused by morpholine, ethylene dichloride, trichloroethane, and the aminated alcohols such as methyl-

diethanolamine.[165] Aniline is another general poison. Its vapour was found to darken the epidermis of *Agriotes* larvae, which is taken to indicate the formation of toxic quinones.[204] Its injection into *Periplaneta* engenders nervous symptoms similar to those of DDT.[136] It has been found to draw out the birefringent particles from the nerve sheaths.[165]

Richards and Cutkomp, in their analysis of insect neuropathology, would prefer to class octyl alcohol and aniline as general poisons and to divide the true nerve poisons into (i) those that act by preferential accumulation in the nerve lipoids, such as pyrethrins, and (ii) those that are specific nerve poisons like atropine and eserine, to which presumably the insecticides HETP and nicotine [165] could be added.

It is of interest that vapours of the insect repellents dimethyl phthalate and oil of citronella are sufficiently toxic to kill *Periplaneta*. The effect of citronella injected into the tracheae was to cause dissolution of the chromatin of the nerve cells. Eugenol, an attractant for *Popillia*, was found to extract the birefringent bodies from the nerve sheath in a manner similar to aniline.[165]

DDT

The highly effective insecticide, dichlorodiphenyltrichloroethane, is a nerve poison whose killing action is comparatively slow. The symptoms in the cockroach *Periplaneta* are characterized by tremulousness of the entire body and its appendages, a condition known as "DDT jitters." The normal gait is uncoordinated, and small stimuli of sound or touch result in exaggerated activity. The insect falls on its back time and again until it can no longer right itself. The legs continue to show high-frequency twitches superimposed on slow spasmodic movements, the twitches disappearing first; these two types of muscular movement are the result of the two kinds of innervation of cockroach muscle. After the slow movements of the extremities finally vanish, the heart continues to beat for some time, and galvanic stimulation may still evoke responses until death supervenes in approximately 24 hr.[209]

DDT poisoning proceeds at a faster rate in the more susceptible species such as the adult mosquito, the housefly, or the honeybee. Characteristically the insecticide is taken up from

residual deposits on surfaces through the feet of these insects. At a temperature of 27° C, the housefly is paralysed $1\frac{1}{2}$–2 hr after contact, the honeybee 2–4 hr after contact.[185] The honeybee so poisoned dies within 12 hr. After a latent period of 30 min, paralysis travels forward from the metathoracic legs, the insect rolling and falling until death.[56] When the honeybee is poisoned by a stomach dose of DDT, death results after 17–42 hr. A latent period of several hours precedes the symptoms of excitation, then ataxia, then a succession of falling and rising. Finally it lies paralysed on its back with only the legs quivering.[93] In the blowfly *Phormia*, prostration succeeds hyperactivity and ataxia within 15–30 min; violent spasms and high-frequency tremors precede death.[17a] Injection of DDT into larvae of *Drosophila* evokes a response within 20 sec; the heartbeat is accelerated, and wave after wave of contraction passes along the longitudinal muscles of the body wall. These contractions, accompanied by short twitches in certain points of the body, persist until death supervenes after 10–30 hr.[9] On the other hand, injected DDT was found to have a negligible effect on the heartbeat of *Periplaneta*.[142]

It has been noted that certain geometrid moths, when poisoned by DDT, lost their legs by autotomy, and that the severed legs continued to show the characteristic tremors.[221] This has occasionally been observed in flies. Experiments performed on *Periplaneta* have shown that the characteristic tremors may be induced by injection of DDT into the severed leg of an untreated insect. If injection is made at the base of the leg, the tremors appearing in the extremities may be stopped by cutting distad to the point of injection. It was therefore concluded that DDT in the relatively high concentrations so applied acts directly on the motor nerves.[233] But if application is made at a concentration of about 5 ppm in the haemolymph, such as would result from a minimal effective dose of 10 mg/kg, DDT exerts no effect on the motor nerves. However, it does set off a series of impulse trains in the sensory fibres of the crural nerve and can do so even when in much more dilute applications.[180] These sensory fibres normally carry impulses from the campaniform sensilla on the trochanters of the legs, and it is probably here that DDT

produces its effects at the lowest dosage level, since excision of the campaniform sensilla is found to inhibit its action on the crural nerve. Moreover, low concentrations of DDT do not affect the normal nervous discharge from spines and hair sensilla.[181] In order to translate the effect on the sensory fibres into symptoms in muscular movement excited by the motor fibres, an intact reflex arc is necessary (Fig. 15). Blocking the ganglion, or physically removing it, completely inhibits the production of symptoms by low doses of DDT, but high concentrations still exert a direct effect. However, the fast twitches, characteristic of the poisoned cockroach, appear only if the reflex arc is intact.[209]

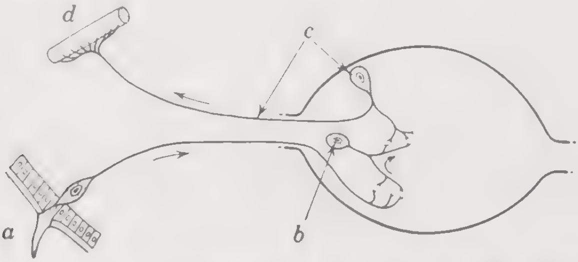


FIG. 15. Diagram of a simple reflex arc. *a*, Sense organ leading to sensory nerve; *b*, association neurone in the ganglion; *c*, efferent neurone forming motor nerve; *d*, muscle. (From Wigglesworth, 1947)

In brief, DDT in low concentration acts on the sensory nerves, whose patternless impulse trains are transmitted to the motor nerves *via* the reflex arc, to produce the characteristic twitches and spasms of the muscles. The effect of DDT on isolated arthropod nerve is to multiply the impulses passing through the treated region, each simple impulse becoming converted into a train or volley of impulses, at a frequency of 250–500 per second, and a duration of 0.1–1.0 sec (Fig. 16). These effects are very similar to those caused by reducing the level of Ca or Mg ions in the perfusing fluid.[181,218] In higher concentration DDT may also act directly on the motor nerves themselves. In very high concentrations it will exert an effect directly on muscle, even when isolated from the nerve.[180] Typically, the action of DDT is restricted to the reflex arc of the segment into which it has been introduced, for injection even into the head will affect the appendages of the head only.[234] At concentrations sufficient to

kill by nervous action, DDT has no effect on the growth of the imaginal discs within fly larvae,[9] or on cells in tissue culture.[11] The highly sensitive ultrastructure of insect nerve is not impaired by DDT, and this poison has not produced any histopathological change in *Calliphora*, *Lucilia*, *Phormia*,[224b] or *Periplaneta*.[165] However, relatively slight changes were noted in the brains of contact-poisoned *Musca*, consisting of partial lysis of fibres and nuclear degeneration,[80] and in the gut of *Apis* orally poisoned by pure DDT [Salkeld, *Can. Ent.*, **83**:39–61 (1951)]. Since DDT has a strong affinity for cholesterol, the suggestion has been made that it acts upon this substance in the lipoid membrane of nerve cells,[112] and thus reduces its permeability to Ca ions.[218]

A
B
C

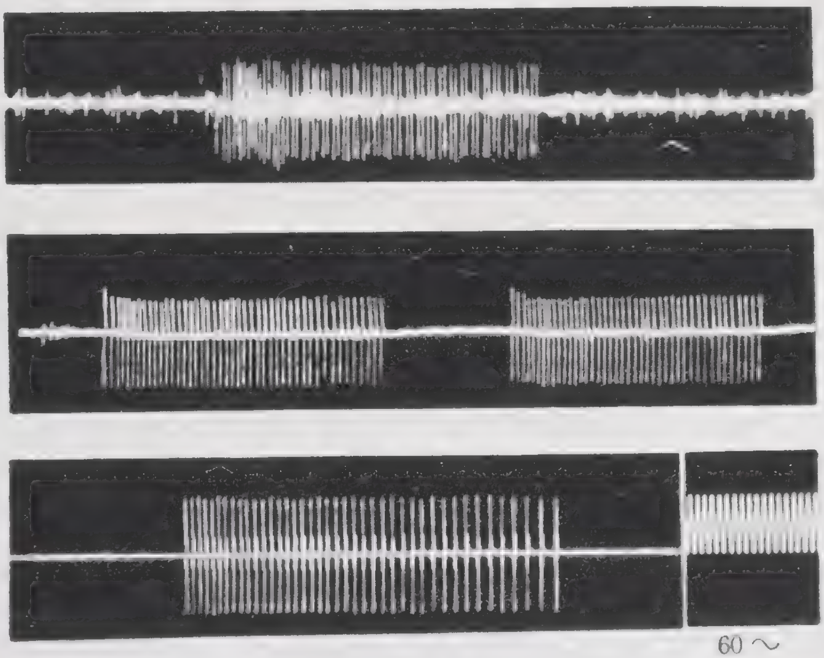


FIG. 16. Action currents of arthropod motor nerves; electrograms of cathode-ray oscillograph traces. A. Poisoned with DDT: repetitive discharge after single brief stimulus, against background of spontaneous activity. B. Spontaneous trains of impulses under DDT poisoning. C. Spontaneous trains of impulses under naphthalene poisoning. Time signal, 60 msec or 0.06 sec. (From Welsh and Gordon)

DDT poisoning elicits its characteristic symptoms when the insect is narcotized by ether, chloral hydrate, urethane, or curare. But their appearance is prevented when the nervous activity of the insect has been previously depressed by application of atropine, or a barbiturate such as phenobarbital or nembutal. Moreover these drugs have the power to abolish the symptoms of DDT poisoning already engendered in the insect.[151] It may be observed that the symptoms of DDT in the cockroach closely resemble those caused by eserine (physostigmine), a drug whose pharmacological action is derived from its inhibition of cholinesterase in nerve. In fact DDT, like eserine, greatly increases the amount of free acetylcholine in nerve;[211] and the effect of DDT is additive to that of eserine. It was therefore surprising to find that DDT did not inhibit *in vitro* the isolated cholinesterase of insect nerve.[166] The suggestion has therefore been made that DDT increases nerve acetylcholine (the eserine effect) not by inhibiting its enzymic removal, but by accelerating its liberation from the bound reserves.[211]

As the insect enters the condition of tremors or DDT jitters, its rate of respiration rises steadily to a peak that is twice the normal level, as shown by results on larvae of *Popillia* and adult *Blattella* (Fig. 17) and on *Oryzaephilus;*[119] the oxygen consumption then decreases until death. A similar respiratory curve is produced by methoxychlor[86] (Fig. 18). The more sensitive *Musca* and *Phormia* increase their respiration fivefold during DDT poisoning.[17a] The DDT-poisoned *Popillia* larvae rapidly lose weight, all their body glycogen is consumed within 2 days, and fat is being oxidized when they succumb. Adults of *Popillia* similarly poisoned die at an earlier stage, before drawing on their fat reserves. Both larvae and adults completely lose their resistance to desiccation; the adults living in a dry aerial environment therefore were found to die of water loss sooner than the larvae living in moist soil.[121] Poisoned *Phormia* adults lose water faster than the normal, and metabolites even more rapidly; the respiratory quotient rises from 0.90 up to 0.96, indicating consumption of carbohydrates. Nevertheless they die before these reserves have decreased down to starvation level.[150] Roaches poisoned by DDT were found to lose 90 per cent of their body glycogen and glucose before death, along with an abnormal

amount of fat, and to show a terminal accumulation of the ketone bodies, acetone and acetoacetic acid.[129] However, there was no evidence that acidosis developed in the DDT-poisoned *Phormia*.[17a]

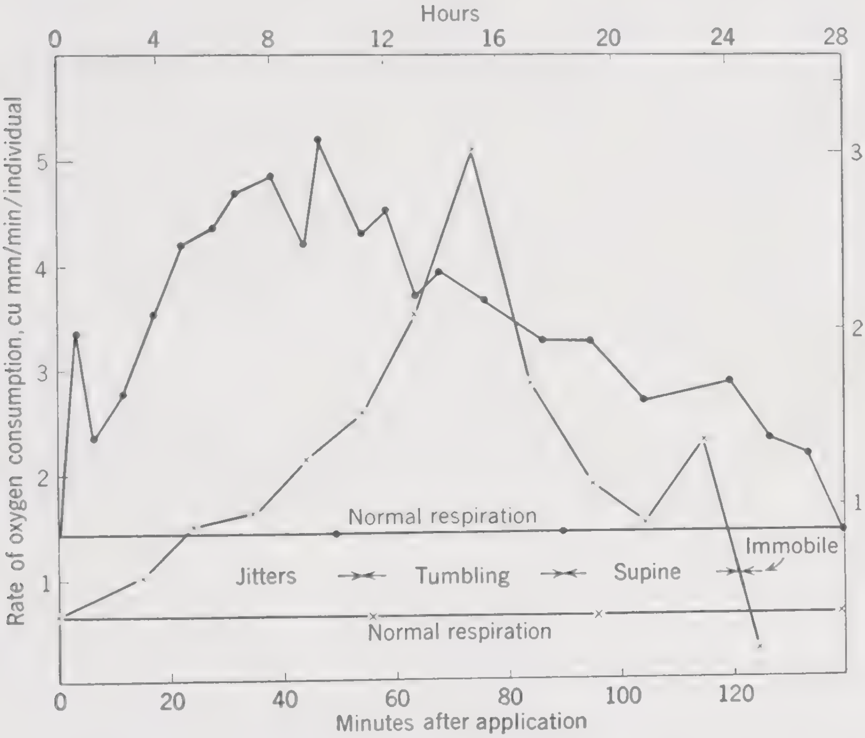


FIG. 17. Oxygen consumption of insects poisoned by DDT. *Upper curve:* adult *Popillia* poisoned with a residual deposit. (From Ludwig) *Lower curve:* adult *Blattella* sprayed with the median lethal dose. (From Harvey and Brown) Upper and right-hand coordinates for *Popillia*. Lower and left-hand coordinates for *Blattella*.

It has therefore been suggested that the DDT-poisoned insect dies from the exhaustion which results from the muscular tetany during the final stage of paralysis, and from intoxication by the metabolites which accumulate in the muscles in their continuous state of contraction.[illegible] The effect of depressants such as atropine or barbiturates would be essentially to relieve the nervous and muscular symptoms long enough for the DDT to be removed from the system by detoxification or excretion (they cannot protect against pyrethrins, which are neurotoxins that also destroy nerve ultrastructure). It has been found that caterpillars may

recover from DDT poisoning if they can be induced to take food during the period of intoxication.[119] The milkweed bug is able to metabolize 80–100% of an injected dose of DDT in acetone at the 100-mg/kg dosage level.[54] DDT-resistant strains of *Musca* have been found capable of rapidly metabolizing DDT (and its *p,p'*-dibromo derivative[224a]) to the dichloroethylene derivative, which the normally susceptible strains are unable to do.[198a] This dehydrochlorination may be largely inhibited by treatment of the insect with piperonyl-cyclonene.[148a]

It is possible that DDT may interfere with the oxidative enzyme system of nerve. Since injection of sodium succinate caused *Calliphora* larvae to recover from DDT poisoning, it has been suggested that the toxicity of DDT is due to the indirect blocking of the succinic dehydrogenase and cytochrome oxidase systems in nerve by its uptake into the phospholipid of the axon sheaths.[99] A number of compounds oxidized by, and used in the histochemical detection of, cytochrome oxidase cause symptoms in the roach very similar to those of DDT poisoning.[136] House-flies treated with DDT exhibit a significant, but incomplete, inhibition of their cytochrome oxidase.*

The outstanding factor in the effectiveness of DDT as an insecticide is that, for a great number of insects, the lethal dose required by contact application is almost as low as the dose by injection, namely about 10 mg/kg.[210] It is as though the cuticle of these insects did not constitute a protective barrier to the entry of this poison. The idea that unsclerotized cuticle does not exclude DDT has been confirmed by the discovery that the purified chitin of arthropods is an effective adsorbent for DDT in solution. Moreover the resistance or susceptibility of the various phyla of the animal kingdom was found to be correlated with the absence or presence of chitin in the cuticle. The susceptible groups were, in addition to insects and crustaceans, those colonial coelenterates that are covered by a chitinous perisarc, and the bryozoans, which possess a cuticle containing a chitinoid material.[167] Thus the insect with its chitinous cuticle collects rather than repels any DDT that is present in its surroundings, whereupon the poison exerts its slow but inexorable derangement of nervous function.

* B. Sacktor. 1951. *J. Econ. Ent.*, **43**:832–838.

Lindane

The gamma isomer of BHC is one of the most toxic insecticides so far discovered. Moreover it is a serious poison for a very wide range of insects; in fact, no insect has been found to be resistant to appreciable doses of it. The recorded median lethal dose by contact varies from 57 to 0.4 mg/kg, depending on the species, a level that may be even lower than the lethal doses by injection.[18, 191]

Since lindane possesses an appreciable vapour pressure at room temperature, it may also enter the insect as a vapour *via* the tracheae, and thus act at a distance from the point of application. This vapour toxicity is not shown by the other isomers, with the occasional exception of the alpha. It is found that an exposure to lindane vapour of between 1 hr and 1 day, depending on the species, is sufficient to cause death. The time of exposure necessary for kill decreases as the temperature rises,[191] so that the Q_{10} for fumigant toxicity in the range 59–86° F is approximately 2.

The following succession of symptoms has been shown by the desert locust (*Schistocerca*) when poisoned by BHC:[145]

Prodromal phase: the abdomen is raised to a position characteristic of anophelines.

Typical phase: the abdomen exhibits telescopic movements, and is rubbed by the hind legs.

Choreo-ataxic phase: the insect is hyperexcitable to stimuli, attempts to fly, and performs an uncoordinated dance.

Clonic phase: the insect falls on its side or back, tremors develop in legs and mouth-parts, and the abdomen may be distended to the point of rupture.

Paralytic phase: insects may copulate as paralysis draws on, before entering the comatose phase.

German roaches on being dusted with lindane became excited within a few minutes and paralysed in 20–40 min, with death following in a few hours. Sprayed houseflies, although not "knocked down" as with pyrethrum, showed typical convulsions in a few minutes, followed eventually by death. Adult *Blattella*

sprayed with the median lethal dose of lindane died within 2.5 hr; whether the insecticide was sprayed or injected, the rate of oxygen consumption of the poisoned insects rose to 6 times the normal during the convulsive period, to fall to twice the normal just before death[86] (Fig. 18). A similar rise in respiratory rate was observed in *Oryzaephilus* to which lindane was applied by contact.[119] The effect of injected lindane on the heartbeat of *Periplaneta* was to induce irregularity in the rate.[142]

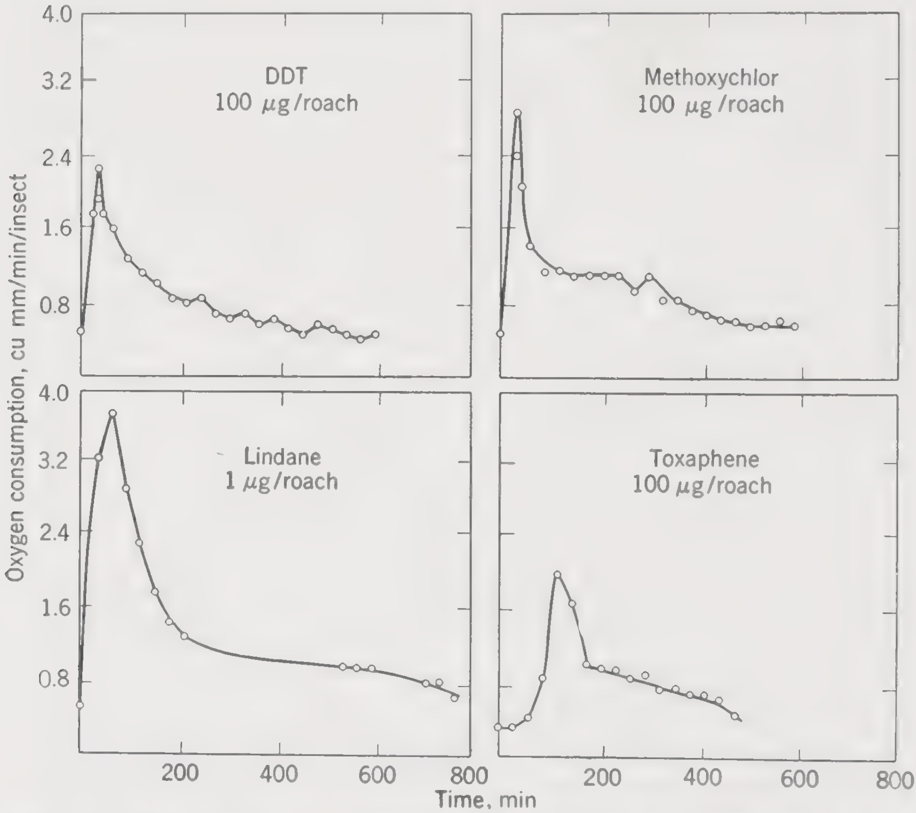


FIG. 18. Rate of oxygen consumption of *Blattella* injected with DDT, methoxychlor, lindane, or toxaphene. (From Harvey and Brown)

The alpha and delta isomers are moderately toxic to insects and to mammals, while the beta and epsilon isomers are nontoxic.[196] Whereas the gamma isomer is a stimulant of the mammalian central nervous system, the beta and delta isomers are depressants and may antagonize the effects of lindane.[158] When applied to *Prodenia* larvae, the delta isomer causes a flaccid

paralysis, whereas lindane causes swelling at both extremities of the caterpillars.[191] When applied to snails, the beta isomer is without effect, the alpha isomer is a paralytic without toxicity, and the delta isomer is a strong paralytic poison, being more effective than lindane presumably because of its greater solubility in water.[75]

The theory has been advanced that lindane owes its toxicity to its structural resemblance to inositol or hexahydroxycyclohexane, an accessory factor for the growth of yeasts and other organisms. Moreover it is considered by some workers to have the same stereochemical configuration as the active isomer (*i*-inositol, also termed *meta*- or *meso*-inositol).[196] This view has received support from experiments on a strain of *Saccharomyces cerevisiae* yeast that requires inositol; here lindane strongly inhibits growth whereas the other isomers are relatively inactive, and the inhibitory effect of lindane may be cancelled by the addition of *i*-inositol.[194] An exactly similar state of affairs was found in the ascomycete fungus *Nematospora gossypii*.[19] However, in the roach *Periplaneta* injection of the LD_{50} of lindane was not cancelled by twice that amount of *i*-inositol,[18] and a parallel result was obtained using rabbits.[128] Nor did mixture of 500 parts of *i*-inositol with 1 part of lindane exert any reduction of the toxicity of lindane to *Heliothrips*.[130] Moreover the position of inositol as an accessory factor in insects is doubtful, as indeed it is in mammals. It has been found to have slight growth-promoting value for 6 out of the 10 species of stored-products insects investigated, but it might have been more indispensable if these insects had lacked symbiotic microorganisms.[65] Finally, van Vloten *et al.* have proposed a new structural configuration for lindane (see Chapter II).

The pharmacological effect of lindane on an insect such as the cockroach resembles that of DDT in that it increases the amount of free acetylcholine in nerve.[211] As a further analogy with DDT, the symptoms of lindane poisoning in mammals may be relieved by atropine and barbiturates.[128] Polychlorocyclane sulphide (SPC), which is a sulphurated analogue of BHC, also causes the typical sequence of excitation, tremors, convulsions, tetany, and paralysis characteristic of a nerve poison.[59]

Chlordane

Technical chlordane is a mixture of isomers of chlorinated methanotetrahydroindanes, of which β-chlordane and heptachlor are the most toxic. The material is an extremely effective poison for heavily sclerotized insects such as locusts, roaches, and ants. The effect of chlordane on *Periplaneta* appears to be that of a depressant, decreasing muscle tonus and causing movements to become weak though still coordinated; high doses have the effect of immobilizing this insect almost immediately. But when in this passive condition, the roach will show exaggerated responses to stimuli. Honeybees become highly agitated on contact with chlordane dust, movements become uncoordinated in 4 hr, and death supervenes in 8 hr.[51]

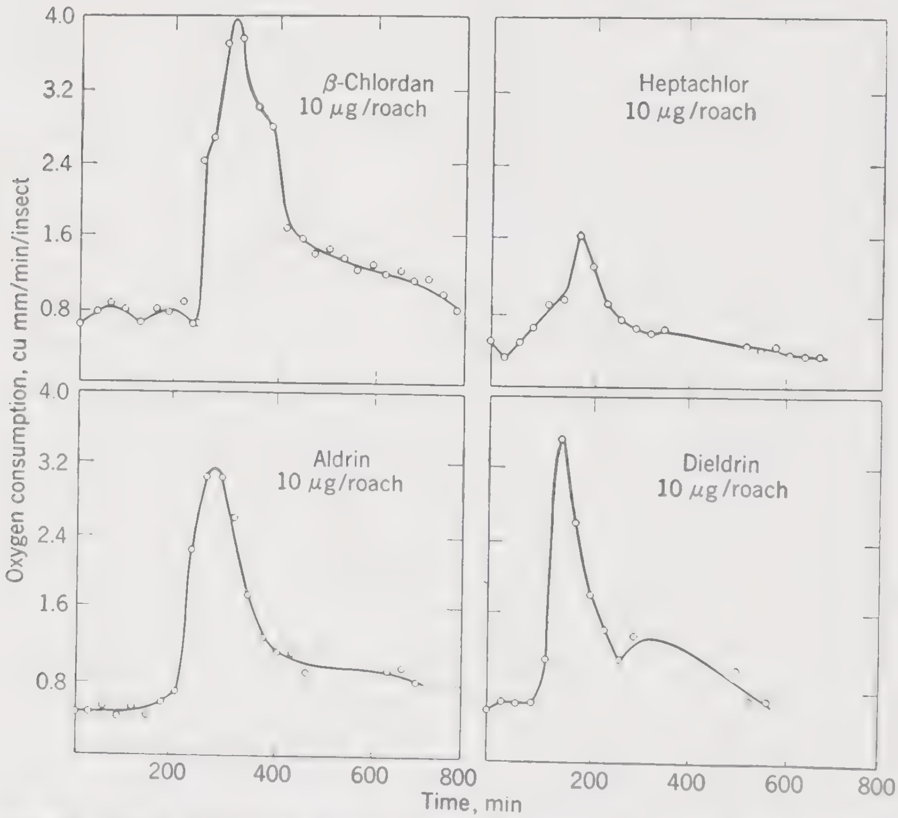


Fig. 19. Rate of oxygen consumption of *Blattella* injected with β-chlordane, heptachlor, aldrin, or dieldrin. (From Harvey and Brown)

The syndrome reported above for *Periplaneta* is reflected in the respiratory picture obtained for *Blattella*. Roaches poisoned with α-chlordane or β-chlordane exhibit a prolonged latent period of 4–8 hr in which the respiration is not increased, followed by a sudden increase (within 10 min) to a peak 5 times the normal level. With heptachlor, however, there is virtually no latent period, and the rise is gradual and less pronounced. With aldrin and dieldrin, there is a latent period of 2–3 hr, followed by a fairly rapid increase to a high peak of respiration[86] (Fig. 19). The heartbeat of *Periplaneta* poisoned by technical chlordane shows a gradual increase in rate.[142]

The action of chlordane on flies is superficially reminiscent of that of DDT, where it has a slow residual action. However, the pulvilli of the feet were found to be much less effective as a route of entry in *Musca* than other parts of the body. This may bear a relation to the discovery that chlordane, being without effect on the roach nerve preparation, is probably not primarily a nerve poison.[176]

Little is known of the mode of action of toxaphene on insects. It has a slight unsettling and stimulating effect on the heartbeat of *Periplaneta*.[142] It increases the respiratory activity of *Blattella* after a short latent period[86] (Fig. 18).

Organic phosphates

Tri-*o*-cresyl phosphate, which is a paralytic drug for higher animals, is a nerve poison for insects also, although it does not show practical insecticidal activity. When applied to *Periplaneta* it induces paralysis and disrupts the ultrastructure of its nervous tissue.[165] *Tenebrio* larvae treated with this compound show ganglionic injury, vacuolization, and tigrolysis, similar to those induced by pyrethrins.[78]

The use of organic phosphates as insect poisons has recently been developed, coincident with the discovery that they exert anticholinesterase activity. The effect of diisopropyl fluorophosphate (DFP) has been studied as both a mammalian and an insect nerve poison. Subsequently the lines of development of mammalian poisons and insecticides have somewhat naturally diverged. The most important compounds to be developed as

insecticides are tetraethyl pyrophosphate (TEPP), which is a constituent of the technical product hexaethyl tetraphosphate (HETP), and diethyl-*p*-nitrophenyl thiophosphate (parathion). Parathion is oil-soluble and shows some residual toxicity, unlike TEPP, which is water-soluble and very labile.

Contact application of HETP to an insect such as the cockroach results in an initial increase in irritability, followed by spontaneous autoexcitation. Subsequently the insect shows violent tremors over its entire body, the legs, wings, and particularly the abdomen all vibrating rapidly; eventually paralysis supervenes. Upon contact with parathion, honeybees immediately become wildly agitated and bellicose, and perform cleaning movements; they become moribund in 30 min.[51] When followed with radioactive tracers in the body of *Periplaneta*, the phosphate is seen to rise abruptly in the haemolymph, and is then concentrated within the fore-gut. The more readily hydrolysed analogues show the greater mobility in this respect. Individuals that succumb have relatively more phosphate laid down in the muscles, while the survivors have relatively more in the fore-gut.[171a]

The toxic effect of anticholinesterases such as HETP and DFP on an insect characteristically takes place at the synapses of afferent and conducting nerves in the ganglia. In *Periplaneta* the 6th abdominal ganglion gathers the sensory nerves from the cerci and connects them with the giant fibres passing up the ventral nerve cord to the brain; here trans-synaptic conduction may best be studied. Perfusion of the ganglion with these anticholinesterase compounds initially facilitates this conduction, thus lowering the threshold of stimulation. Then complete blocks of transmission, about 1 min in duration, alternate with the facilitation. An increase in the concentration of the poison, or the addition of acetylcholine, will effect a continuous block of transmission.[177,178] It has been demonstrated that HETP is capable of inhibiting all the cholinesterase in the nervous system of *Periplaneta*.[28] The effect of HETP and TEPP on the circulatory system and isolated organs of mammals resembles that of eserine and neostigmine.[36]

It has been stated that the alkyl fluorophosphates affect no other enzymes than cholinesterase and other esterases.[17] The

suggestion has been made, without supporting evidence, that the ethyl phosphates and pyrophosphates are toxic because of the formation of diethylphosphoric acid, which may block the process of phosphorylation of carbohydrate by the coenzyme adenosinetriphosphate.[77] However, the insecticidal activity of a long series of organic phosphates has been found to parallel their anticholinesterase activity.[132a]

Parathion, as shown by its action on mammalian brain tissue, is also an anticholinesterase compound. It inhibits the cholinesterase of *Periplaneta* both *in vitro* and *in vivo*. Its pharmacological action on mammals has been compared to that of muscarine,[4] and it is antagonized by atropine, eserine, or magnesium sulphate. Its effect on the nerve of *Periplaneta* was found to resemble that of DFP in causing synaptic block alternating with facilitation. But in low concentrations where DFP is still active, parathion exerted no effect on nerve.[176] Nevertheless, the onset of symptoms of parathion poisoning in the bee can be directly correlated with the extent of cholinesterase inhibition in the victim's brain. Parathion resembles DDT and BHC in that the cuticle interposes no barrier to its entry, the lethal dose by contact being almost identical to that by injection. However, pretreatment with atropine has no effect in protecting *Periplaneta* against parathion poisoning.[132] Like TEPP, parathion raises the respiratory activity of the poisoned roach, but there is a 2-hr latent period, which is lacking in the case of TEPP.[86]

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CHAPTER V

Equipment Developed for the Application of Insecticides

Dispersal of insecticides

The efficiency of an insecticide applicator lies in its ability to kill the maximum number of insects with the minimum amount of insecticidal material. In practice, many hundreds or thousands of times more insecticide is applied than the amount represented by the sum of the minimum lethal doses of the victims. It may be calculated that a population of 1,000,000 adult mosquitoes to the acre requires a minimum of only 30 mg of DDT (1 million $\times$ 3 $\times$ 10^{-2} μg) for their total destruction, provided every trace of insecticide finds its target. The application of DDT at 0.2 lb/acre, the most modern and efficient method, represents an expenditure that is 3000 times this amount.

More precisely, the efficiency of an applicator depends on its ability to distribute the insecticide material as evenly as possible. In fumigation this is an automatic process, since the gas molecules attain a uniform concentration throughout the closed space in which they are liberated and mixed. Similar conditions may be attained in the control of aquatic insects, where diffusion in the aqueous medium may stabilize the concentration at an even

level. The application of non-volatile insecticides to aerial or terrestrial insects becomes a problem of atomizing them into particles or droplets, sufficiently numerous that the victims cannot avoid contacting a lethal dose, yet not so small as to flow around an insect without contacting it.

The advantage of fine atomization for the control of aerial insects has been demonstrated in the standard Peet-Grady test, performed with 0.1% solutions of pyrethrins in oils, against adult houseflies. At a given dosage, raising the atomization pressure from 12.5 psi (lb sq in.) to 25 psi, and thus correspondingly reducing the droplet size (see below), raised the mortality from 36% to 45%; decreasing it to 2 psi gave only 15% mortality.[57] Whereas only 5% of the standard Peet-Grady spray remained airborne 5 min after application, as much as 50% of a very fine spray or aerosol remained in the air, and this figure was still 20% after 20 min.[101] With houseflies it has been determined that the optimum droplet diameter for maximum economy of the insecticide is 22 μ.[115a] With smaller insects this figure is lower, the optimum droplet diameter for killing mosquitoes being 16 μ. However, with aerosols emitted into still air, the higher settling rate of droplets above 20 μ in diameter becomes a factor in reducing the airborne concentration of insecticide, and these droplets are therefore considered to be wasteful of material; with droplets below 2 μ in diameter, their diminished ability to impinge upon the insects renders them undesirable.

TABLE 1. Droplet Size and Toxicity of DDT Aerosols to Mosquitoes

Milligrams of DDT producing 50% mortality of female *Aedes aegypti*[69]

Droplet Diameter,	Milligrams of DDT Required at Following Wind Speeds:			
μ	16 mi/hr	8 mi/hr	4 mi/hr	2 mi/hr
1.1	18.4	126.0	184.0	80.5
2.5	2.35	5.90	14.2	32.0
4.5	1.15	1.29	3.45	10.3
7.0	1.44	2.20	1.90	3.49
10.0	0.59	1.94	2.48	2.08
13.0	0.70	0.70	0.70	0.70
17.8	0.83	1.41	1.31	0.99
20.4	0.87	0.87	0.87	0.87

When an aerosol is moved horizontally in a wind tunnel past adult *Aedes* mosquitoes, the very small droplets are found to be comparatively ineffective because they are carried around the insect in its flow streamlines. If, however, their momentum is reinforced by increasing the rate of air movement, a higher proportion of these minute droplets impinges upon the insect and thus they become more effective. With 2.5 μ droplets moving at 2 mi/hr, enough to contain 32 mg of DDT must flow past the insects to kill 50% of them; when the air movement is increased to 16 mi/hr, the same mortality may be achieved with enough droplets to contain only 2.4 mg of DDT (Table 1). If the droplet size is increased to 20 μ, this LD_{50} dose falls to 0.87 mg; it is not affected by wind speed, for even in light winds the droplets have sufficient momentum to give the maximum impingement of which they are capable. Within the range of droplet sizes small enough to require increased movement to attain more deposition, the effectiveness is proportional to the air speed and the square of their diameters D^2v, until it reaches a maximum where $D = 13\ \mu$ and $v = 5$ mi/hr, or where a 10 μ droplet is moved at 8 mi/hr (Fig. 1). The LD_{50} for an adult *Aedes* mosquito was found to be 3×10^{-2} μg of DDT, which is the amount contained in an 83 μ droplet of a 10% solution, or 572 droplets 10 μ in diameter.[69]

Experiments have been performed to investigate the effectiveness of an aerosol settling by gravity on adult *Aedes* mosquitoes, and to express the results in terms of the product of the concentration (C) of insecticide and the time of settling (t). It was found that the Ct (in mg-min/m^3) necessary for 50% kill was as much as 1700 when the DDT was applied in 0.7 μ droplets, whereas it was only 4.2 when 11 μ droplets were employed. This result is due to the simple fact that more material settles on the mosquito in a given time t when it is in larger droplets than when it is in the form of smaller droplets. The increase in effectiveness is found to be directly proportional to the square of the droplet diameter, D^2, just as the settling rate by Stokes's law is a function of D^2. When the droplet size is increased beyond 11 μ the effectiveness decreases, in spite of a higher settling rate, for the reason that for a given C the droplets are farther apart and the element is introduced of chance hit-or-miss upon the insect.[69]

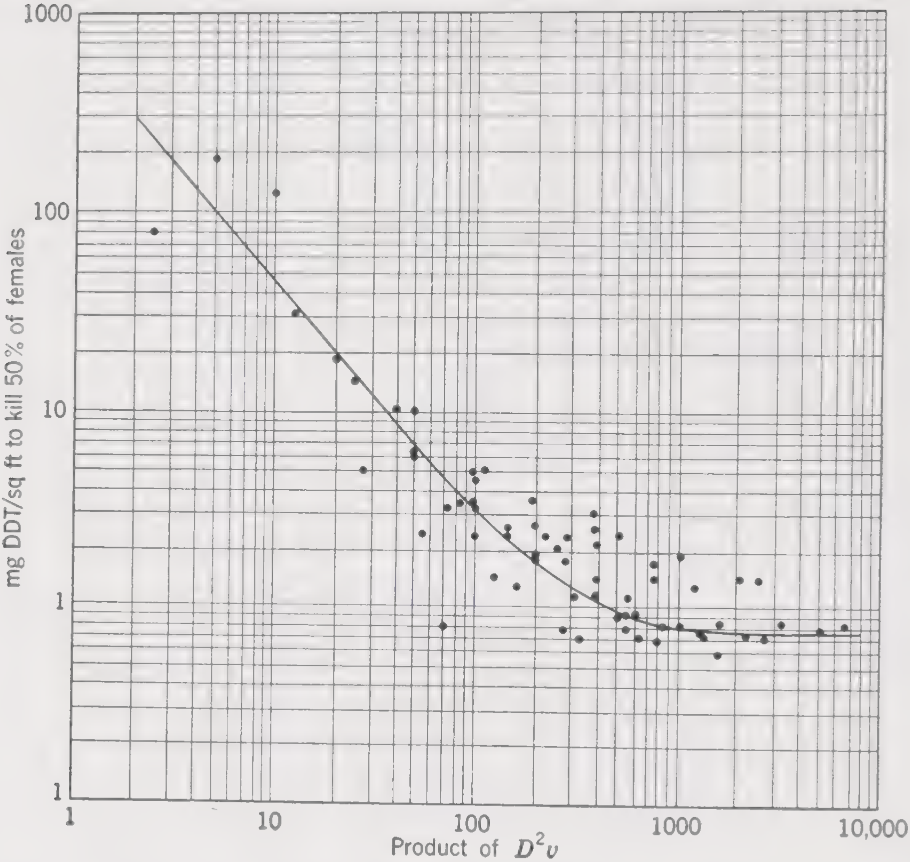

FIG. 1. Relation of droplet size and velocity to the toxicity of aerosols. Plot of D^2v against median lethal concentration of DDT for *Aedes* females. (From Latta *et al.*)

Flying mosquitoes collect a great deal more of the insecticidal droplets than do mosquitoes at rest. For a given spray of DDT, the mortality of *Aedes* may be increased from 14% when at rest to 63% when the mosquitoes are agitated into activity.[31] The mortality may also be increased if the air is moved past the insects at a higher rate. It has been found that the wings while in motion collect about 5 times as much spray material as the body does, and the insecticide is absorbed directly or transferred to the mouth by cleaning movements.* Amputation of the wings greatly decreases the mortality rate. Similar results have been

* The legs are also spread wide in flight and are efficient aerosol collectors (Walton, Porton Tech. Paper 12, 1947).

obtained with the adult housefly.[30] One of the effects of the inclusion of pyrethrins in fly sprays is to activate the insects to collect more of the dose.[76]

Impingement of droplets upon obstructions. A knowledge of this process is important not only to establish how much material is deposited upon the insects themselves; it is also pertinent to determine how much is deposited upon vegetation to give residual toxicity, or alternatively to establish to what extent a direct-contact aerosol is diluted by the screening power of obstructions.

It is known that when an air stream approaches the side of a cylinder, the frontage of air matching the cylinder diameter is split into two streams which pass on either side, such that the sum of their cross sections is only about 75% of the original frontage. The speed of the air in the streamlines is correspondingly increased to balance the decrease in frontage. It has been found that droplets which approach the cylinder in the exact centre of the air stream, i.e. for a frontage width amounting to 1.5 times their diameter, fail to clear the obstruction even although they may follow the streamline flow exactly. This direct filtering effect generally involves a very small proportion of the droplets that impinge. Small droplets approaching on either side of this minute central strip flow with the air around the obstruction. Larger droplets, however, have sufficient linear momentum or inertia to resist the angular change in direction during their acceleration around the obstruction; they fail to be sufficiently diverted from their course and therefore impinge upon the cylinder. The larger the droplets and the greater the speed at which they approach, the less the directional change that can occur, and the greater the amount of impingement. When the diameter of the cylinder is increased, a smaller angular change is sufficient for the droplets to avoid the obstruction, and thus a smaller proportion impinges upon it. The existence of this boundary layer of moving air around obstructions, through which the droplets have to penetrate in order to impinge, has been responsible for the idea of a "layer of resistance" around objects in an aerosol stream.

The efficiency of an obstruction to filter out droplets by impingement is measured as the dynamic catch, or E_m, which is the

fractional width of the approaching stream which is cleaned of droplets. A cylinder ⅛ in. in diameter shows an E_m of 32% for 10 μ droplets approaching at 10 mi/hr. If the speed of approach is raised to 50 mi/hr, the dynamic catch rises to 85%; alternatively, if the particle size is increased to 20 μ, the efficiency becomes 65% (Fig. 2). A complete cleaning of the entire ⅛-in. width of the approach stream (i.e. $E_m = 100\%$) is obtained with 100 μ droplets approaching at 50 mi/hr.[21]

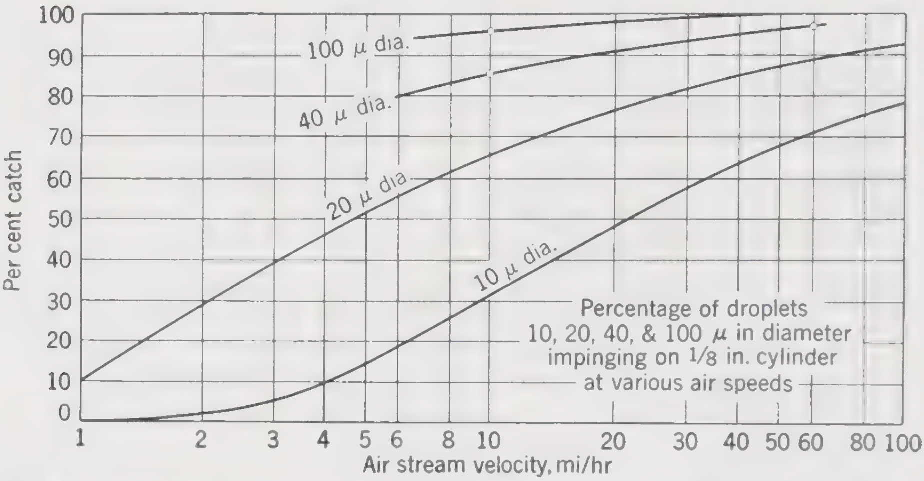

FIG. 2. Relation of droplet size and wind velocity to the dynamic catch of aerosols. (From Brooks)

A spherical object interposed in a moving aerosol achieves a lower dynamic catch than a cylinder, whose surface is flat in one dimension; a plate, which is flat in two dimensions, collects more than a cylinder. An increase in cylinder diameter, besides decreasing the deposit on the upwind side, increases the deposit on the lee side; the lee deposit is also increased with wind speed. With spherical objects, more is deposited on the back than the front at low wind speeds, but more on the front than the back at high wind speeds.[58] The smaller droplets tend to be deposited more on the backs of obstructions, larger droplets more on the fronts; at a wind speed of 8 mi/hr, the division between larger and smaller droplets on this basis occurs at the diameter of 16 μ.[115a]

It has been observed that for an aerosol to penetrate forested areas to kill mosquitoes, the droplets must be smaller than 30 μ

in diameter to prevent excessive filtering by foliage. For penetration through thick jungle, it has been considered that the droplet size should be below 10 μ. If, however, the aerosol is applied to forest from aircraft with the aid of the downdraft of the wing airfoil it will penetrate so long as the droplet diameters do not exceed 50 μ. When emitted from generators on the ground, droplets of more than 40 μ diameter do not remain airborne for a sufficient distance to be useful. An increase in wind speed enables the larger droplets to be advantageous; for mosquito larviciding, the optimum droplet size for a 1- to 3-mi/hr wind is 16 μ, for 3- to 6-mi/hr winds it is 24 μ, and for 6- to 10-mi/hr winds a diameter of 32 μ is optimum.[20]

When an aerosol is emitted in the open air to travel downwind, much of its effectiveness may be lost by its rising to heights which are not inhabited by the target insects. This rise is largely a consequence of upward convection by turbulent air, which occurs during the day when the air at the surface of the ground is warmer than the overlying levels. It has been recommended that heat-generated aerosols should not be applied in the field when the temperature of the air at 3 ft above ground is more than 5° F warmer than the air 20 ft above ground. This is the maximum amount of "lapse" that is tolerated.[8] When penetration into coniferous forest is required, the wind speed in the open should not be less than 5 mi/hr.

The distances that an aerosol is carried both upwards and sideways by vertical and horizontal convection are functions of the horizontal and vertical gustiness coefficients (G_z) of the air.[21] With small-scale convective turbulence the vertical G_z is 0.10 and the horizontal 0.160; with the onset of normal stable air in the evening these values fall to 0.04 and 0.054, respectively. Under very stable conditions and with a 3-mi/hr wind, a dust aerosol emitted from a point source and travelling downwind will spread horizontally in a crosswind direction in such a manner that the boundary where the concentration is 10% of that at the midline moves outwards at a speed of 17.5 ft/min; in unstable afternoon conditions this outward spread occurs at a speed of 95 ft/min, because of the horizontal gustiness being very much greater. The resultant contours of aerosol concentration over the ground surface are shown in Fig. 3 for both types

of atmospheric conditions. The dissipation of concentration in an upward direction bears the same type of relationship to vertical gustiness.[21]

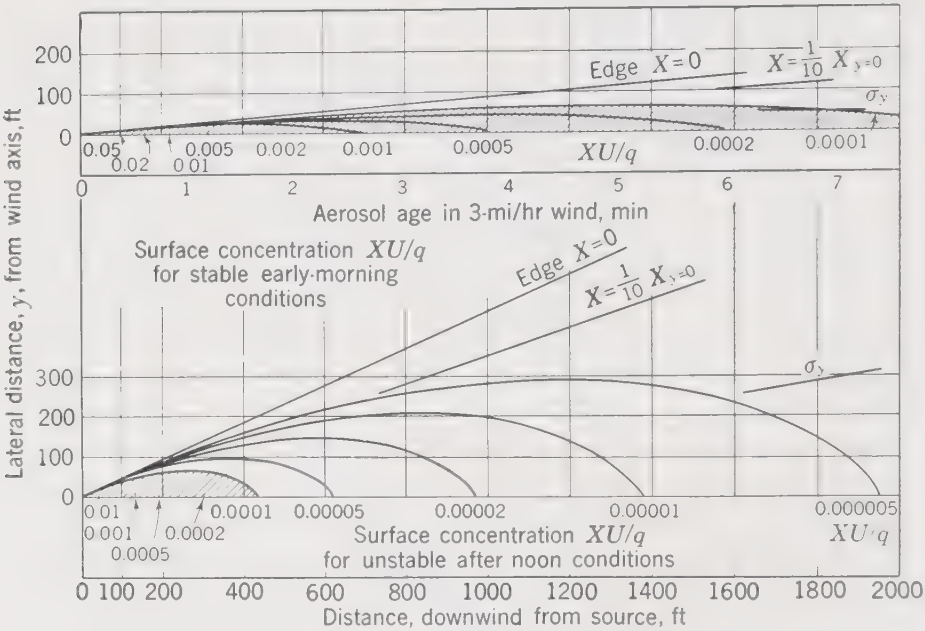

FIG. 3. Dispersal of a dust aerosol downwind of a point source. Contours of concentration over ground surface. *Upper plot:* very stable air. *Lower plot:* small-scale convection conditions. (From Brooks)

Spraying and dusting

More frequently the problem of application is to make deposits on horizontal surfaces, either to contact resting insects or to leave a residual deposit for them to contact or eat. For modern application this becomes a problem of leaving a continuous film of the minimum thickness possible, for with the potency of the new insecticides there is little fear of there not being enough poison. The main source of inefficiency in application is the existence of gaps, between the deposited droplets or particles, of sufficient size that the victim will escape. Contact insecticides against aphids have a target 0.6 sq mm in area. Stomach insecticides against white pine weevil are aimed at a feeding hole 0.8 mm in diameter.[89]

When droplets of aqueous sprays are deposited on plant surfaces, their diameter increases up to 3 times; oil droplets spread up to 10–15 times their original diameter. However, this spread

factor is lower the larger the droplet size. To form a continuous film on an acre of foliage with 1 gal of oil, only the smallest droplets are sufficiently numerous to coalesce continuously. The number of droplets falling on a unit area decreases from about 10,000 per square inch when their diameter is 50 μ, down to only 40 when their diameter is 300 μ (see Table 2). Since the area of leaf surface presented vertically in an acre of vegetation is many acres, the coverage per unit of leaf surface will be considerably less.[89]

TABLE 2. THE EFFECT OF ATOMIZATION ON COVERAGE [89]

Number of droplets per unit area for an application of 1 gal/acre

Diameter, μ	Volume, cu μ	Number per sq mm	Number per sq in.
10	525	1,780	1,148,100
20	4,200	222	143,190
50	65,520	14.3	9,224
100	525,000	1.78	1,164
200	4,200,000	0.22	142
300	14,175,000	0.066	43
500	....	0.014	9

There is a lower limit to the optimum size of droplets for deposits on vegetation, since the smallest droplets do not have enough momentum to impinge upon it. In addition the finest droplets are more subject to drift away from the target by horizontal wind or upward convection, because they remain airborne longer. They are also more susceptible to loss of volume by evaporation. Substances of the volatility of water are particularly susceptible to this loss, unless a hygroscopic solute is added (e.g. a hexahydroxy alcohol, *Yumidol*). Wetting agents are ineffective in reducing evaporation;[58] on the contrary they increase atomization.[89]

It has been the general experience of field workers that the optimum droplet size for coverage by ground applicators is from 80 μ down to 30 μ. Sprays applied from aircraft (falling from 5 to 25 ft with turbulence) require a larger droplet size to prevent drift, namely 70–100μ.[89]

Droplets once produced in a spray by an air atomizer do not coalesce again. When liquids are sprayed into each other by convergent air-atomizing nozzles, there is no measurable agglomeration of droplets in the region where the high-velocity air

stream from the nozzle expands and slows down.[58] But with hydraulic-pressure emission, the finer droplets are expected to be picked up by the larger droplets moving past them with greater momentum. It is generally considered that agglomeration does not occur when droplets are moving with gravity or with the wind. However, the aggregation of aerosol droplets has been reported in wind-tunnel studies, particularly in the eddy behind objects placed in the air stream.[58]

When wettable powders are applied in aqueous suspension of approximately 0.1% concentration, the amount required for adequate coverage is of the order of 100 gal/acre, varying according to the crop. When the insecticide is applied in oil solutions from aircraft, in concentrations of approximately 5%, an area dosage of about 2 gal/acre is sufficient; a similar result may be obtained if concentrated suspensions are employed. Mosquito adulticide sprays are applied at 0.5 gal/acre, and aerosols at 0.1 gal/acre. Increasing fineness of atomization (up to a certain point, corresponding to a droplet size of about 30 μ), and decreasing volatility of the carrier, allow ever smaller amounts to achieve adequate coverage on foliage. It is probable, however, that oil should never be applied at less than 1 gal/acre and water at less than 50 gal/acre.

Dusts are usually applied in amounts between 30 and 50 lb/acre, although dosages ranging up to 100 lb/acre may be employed for certain crops. Increasing the percentage of the insecticide in the dust reduces the total amount of material required; DDT applied at 1.2 lb/acre gives similar results against corn borer whether applied in 3%, 5%, or 10% dust.[34] Thus, within the normal range of concentration for dusts and sprays, it is comparatively unimportant how much total material is applied so long as the amount of insecticide is maintained at the correct level. Experiments conducted on *Epilachna* and *Pieris* showed that the total dosage of dust could be reduced to 10 lb/acre and still be as effective as 80 lb/acre provided the amount of insecticide (rotenone or cryolite) was maintained.* In reducing the dosage per acre to an economical figure, the

* However, Lord [*Ann. Appl. Biol.*, **37**:123 (1950)] has found that, for a number of insecticides against *Tribolium*, a change in the concentration of dust has a much greater effect on the results obtained than a change in the amount of dust.

control decreases less when the total amount rather than the insecticide concentration is reduced.[104] The substitution of impregnated dusts for straight-mix preparations allows half as much insecticide to be applied with the same results.

Insecticidal dusts when emitted from a blower consist of a mixture of discrete particles, with agglomerates which may consist of as many as 25 or even 300 coalesced particles. This factor of agglomeration leads to wide variation of settling characteristics even in a dust of uniform fineness of grind. In addition to size, the shape and specific gravity of dusts are important in deciding their settling characteristics. Particles of high density such as barite or lead arsenate show good deposition on foliage, whereas derris and pyrethrum dusts, whose particles are light and angular, give poor deposits. Cryolite dusts deposit poorly because they show very little agglomeration.[59] The fractionation of dusts during the settling process may also separate the insecticide from its diluent. Dusts are deposited better on foliage nearer the blower than at greater distances, and more permanent deposits are produced with a strong air blast than with a weaker one.[57]

The electrostatic charges which dusts may assume introduce a factor of uncertainty in their deposition. All inorganic materials tested (arsenicals, fluorine compounds, sulphur) were found to assume a positive charge, regardless of the type of metal in the applicator. The botanical insecticides (derris, sabadilla) were found to assume a negative charge.[111] Charged particles may produce an uneven deposit on plants and may stand out on the insects' integument like iron filings on a magnet.[110] A dust diluent such as pyrophyllite assumes a positive charge, which may be reduced to zero if derris is added to it in equal proportions.[104] Gypsum was found to resemble pyrophyllite in being attracted to a negatively charged plate, whereas diatomite, clays, and talc were attracted to the positive plate.[77a] The electrostatic charge on leaf surfaces, which are claimed to be negative, affects the deposition of dusts but not their adherence.[79a] Gypsum, bentonite, and clay absorb moisture, but it does not increase their adherence; talc does not absorb moisture.[37]

Dusts fall into three fractions according to their behaviour in air: (i) coarse heavy particles which fall almost vertically, (ii) intermediate particles that fall more slowly with a swirling motion, and (iii) light particles which settle very slowly in a fine

cloud. The bulk of the particles in gypsum dust belong to class i; in talc the particles mostly behave in class iii.[57] Dusts are typically so fine and light that they are very sensitive to wind. When calcium arsenate is applied at 22 lb/acre (20 kg/hectare), an increase in wind speed from 1.4 mi/hr to 4 mi/hr decreases the average deposit on the treated field from 130 mg/m² down to 90 mg/m².[92] In the case of this insecticide especially, the hazard of the material that drifts out of the area is more serious than the decrease in deposit within the area. The amount of drift may be reduced by the addition of oil or water to the dust as it is emitted, since these liquids promote the agglomeration of particles while in flight. Although this measure does not always increase the degree of deposition on the target foliage,[79] it does increase the adherence of the dust once it is deposited.[59] Moreover, the addition of oil to DDT dusts increases their adherence to the smooth cuticles of insects.[314]

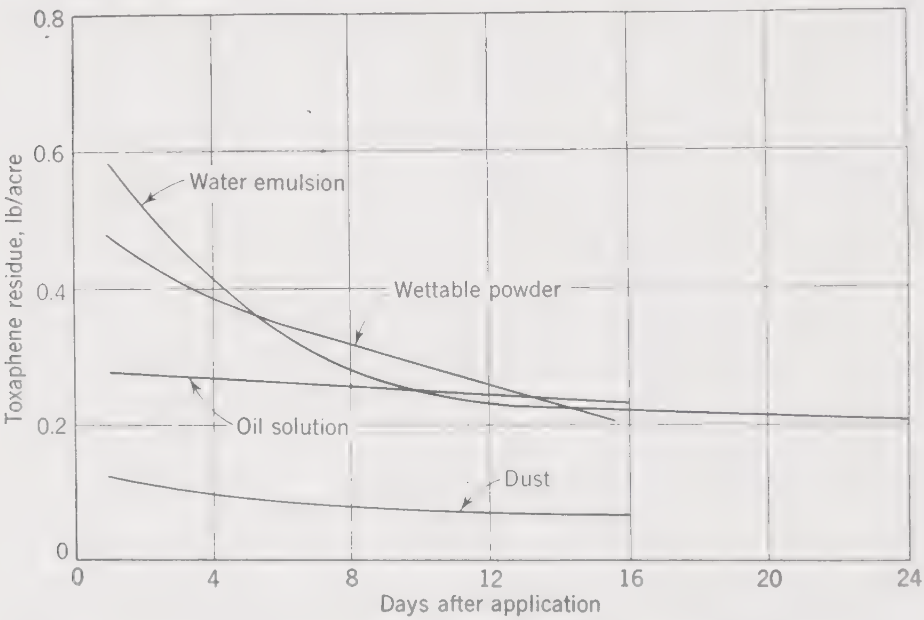

Fig. 4. Deposit of toxaphene on alfalfa hay and subsequent decline in residue concentration. Insecticide applied at 2 lb/acre in 4 different formulations. (From Laakso and Johnson)

Although residues from dust deposits show a surprising persistence, the initial deposit is light as compared with that obtained from sprays (Fig. 4). When toxaphene was applied to

alfalfa in four different formulations, the percentage of material applied that was recovered in deposits on the plants 1 day after application was 7% for dusts, as compared with 14% for oil solutions, 24% for suspensions, and 29% for emulsions. Within 16 days the residues from all three spray applications had decreased to an equal figure equivalent to 11% of the amount applied.[64a]

Nozzles

When a liquid is extruded under pressure from a single orifice, it emerges as a pencil until it loses its original velocity and its motion under gravity takes over. The slightest displacement causes constrictions and bulges, which eventually are pinched off as droplets. When the larger droplets separate, the last thin connecting filaments break up into very small droplets.[64] Simple orifices have a place in insecticide spraying only when combined with an air blast or other fast air movement, as in a turbine sprayer or a straight emission pipe in a fast aircraft. The impact of high-velocity air alone is sufficient to pull out filaments of liquid, which then break up into very fine droplets; this is the principle of the air atomizer. A small proportion of the energy required for atomization is needed to overcome the surface tension of the liquid. The major energy requirement goes towards overcoming the viscosity of the liquid, which opposes its deformation into droplets. Hydraulic pressure offers an efficient source of energy; compressed air or steam can constitute a much greater reservoir of energy, but its application to the fluid is inefficient.

TABLE 3. Droplet Diameters Obtained with Whirl-jet Nozzles on Knapsack Sprayers [86]

Median diameters (by number) in microns.

Pressure, psi	$\frac{1}{16}$-in. Orifice		$\frac{1}{32}$-in. Orifice	
	Water	Kerosene	Water	Kerosene
25	168	290 *	163	185
50	151	175	141	147
75	147	163	119 †	148

* Largest droplet 400 μ.
† Largest droplet 250 μ.

If the liquid is made to rotate before leaving the orifice, it will spread out into a hollow cone bounded by a sheet of liquid. The rotating hollow cone of spray breaks up into threads, and finally into droplets.[86] The momentum of the larger droplets creates an air current which serves to carry the fine droplets. This condition may be produced by the **swirling-jet nozzle** type, such as is used on knapsack sprayers, where it gives rather a coarse spattering spray.[52] The spiral motion is imparted to the liquid by a fixed screw thread fitting within the delivery pipe, which leads into a length of whirl chamber before reaching the nozzle. A slotted plate will give the same rotating effect. In swirling-jet nozzles, the diameter of the orifice (unlike air-mix nozzles with eddy chambers) affects the droplet size, smaller orifices giving finer sprays (Table 3). Where the orifice is small, and the spray liquid is delivered directly to it by a screw thread, the model is a **vermorel nozzle.**[1] This delivers fine sprays at reasonably low pressures; the inner threaded screw is tipped with a disgorger pin to open the orifice in case of clogging[90] (Fig. 5).

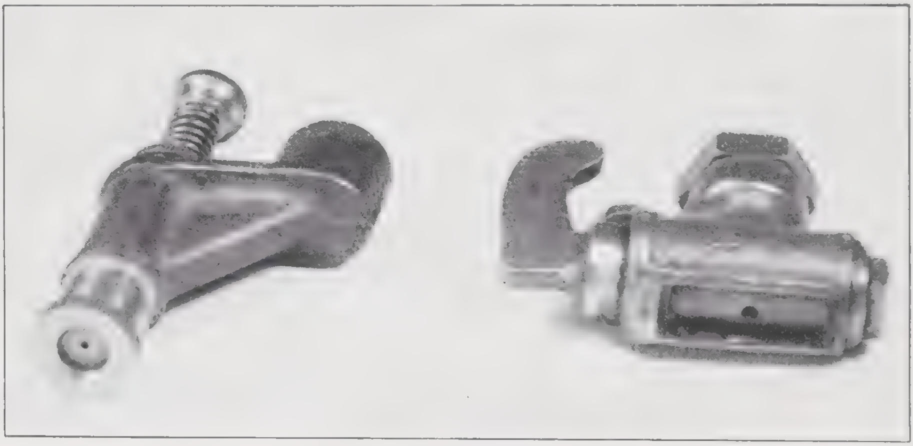

FIG. 5. Vermorel nozzle (*left*) and Bordeaux nozzle (*right*).

The break-up of liquid may be increased by the insertion of a disc within the whirl chamber, past the circumference of which the liquid has to force its way against air pressure. An example of such an impact nozzle is the **disc nozzle**, a familiar attachment for garden hose, where the chamber is long and narrow, along which a lens-shaped disc is moved by an adjustable plunger. When the disc is placed beyond the final orifice, a wide-angled

spray results from the deflection it imparts; when it is withdrawn into the chamber, a narrow jet is produced. The spray becomes finer as the disc approaches the orifice from either direction. In the **fern nozzle,** the disc is held some distance in front of the orifice by embracing metal arms, and its surface is convex so that the impinged liquid flows to its circumference, where the atomization takes place. Fern nozzles are constructed for emission rates from 0.1 to 1.5 gpm (gal/min).

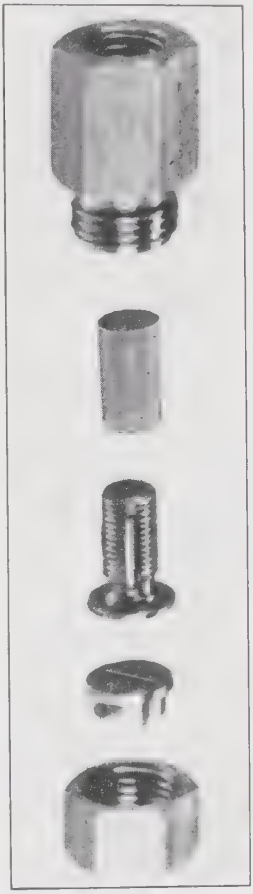

Fig. 6. Disassembly of flat-spray nozzle. (Courtesy of Communicable Disease Centre, U. S. Public Health Service)

In **flat-spray nozzles,** two streams impinge on one another in the chamber just before they pass through the orifice, thus producing a thin fan of liquid. This type of emission has little carrying power; it may be increased by a central stream, which thickens the fan but simultaneously decreases the atomization.[32] The more modern flat fan-spray nozzles have a milled cut or channel behind the orifice plate; and the orifice may be oblong, lying in a groove running along the nozzle cap. There is no eddy chamber, but simply a length of tube in which the strainer sits (e.g. *Teejet*); thus the atomizing power is low[7] (Fig. 6). Also the edges of the fan may be thicker and may constitute "horns" which give large droplets and may contain a high proportion of the spray.[56] This results in a coarse, driving, biting spray as is needed in weedicide work. Fan-type nozzles are suitable for boom sprayers where little force is needed, and since they normally range from 1.6 gpm down to 0.03 gpm or less, they are well adapted for low-volume wide-angle emission. The angles included by the fan usually range from 65 to 80°, depending upon the construction; there are special nozzles whose included angle is 100°, with emission greater on one side (*Boomjet*).[7] Since an increase in pressure widens the fan, specifications are quoted for a given psi figure.

In **mixing nozzles** the extruded liquid is subjected to disruption by air before it finally leaves the orifice. This occurs in an expansion chamber, the so-called eddy chamber, whose diameter is considerably larger than the entrance and exit. A simple example is the **jet nozzle,** which is flask-shaped and contains a removable inner core with spiral flanges which impart a swirling motion to the liquid and break it up into coarse droplets before it leaves the orifice. A central axial jet is usually added whose impact on the rotating fluid just behind the orifice causes the atomization and fills the centre of the hollow cone[36] (e.g. *Fulljet*).[5] This type of jet allows for high emission rates, from 1 gpm up to 500 gpm, and may be used on large aircraft sprayers.[97]

In **hollow-cone nozzles** a vortex plate is inserted in the floor of the eddy chamber. It is perforated with a number of spirally or tangentially arranged channels, which cause the liquid to whirl around the chamber before passing through the orifice. Thus the liquid debouches into the outer air as a rotating hollow cone, which appears first as a continuous sheet, then as threads, and finally as droplets. Yet in this case it is the size of the vortex openings and eddy chamber, and not the orifice, which determines the amount of atomization and the resulting droplet size. The smaller the channels which perforate the vortex plate, the finer the spray.[32] A point may be reached where the vortex openings and the eddy chamber are so small that there is no atomization at all.[70] Deepening the eddy chamber results in a coarser spray or even a jet-type stream; restricting it by advancing the vortex plate towards the orifice produces a finer spray and a wider cone, and the rate of emission is simultaneously reduced. In the adjustable nozzles installed on spray guns, the vortex plate may be moved by a plunger; or a fixed vortex plate may be by-passed, for solid-stream spraying, by screwing back the plunger which forms an integral part of it (Fig. 7). Nozzles designed to carry spray for long distances have an extremely long eddy chamber. The shade-tree guns are as much as 50 in. long and their orifices are ¼ in. in diameter.

A hollow-cone nozzle, when aimed at a flat target not more than 3 ft away, will deposit the spray droplets in the form of a ring. If a central perforation is inserted in the vortex plate, of

approximately the same diameter as the nozzle orifice, this ring is filled in to give a solid cone of spray which deposits in the form of a disc. **Solid-cone nozzles** allow a faster delivery, but the coverage they give is not a significant improvement over the hollow-cone nozzles when used on guns or brooms where the target is more than 3 ft away, since air-current disturbances over-ride the spray pattern. At distances of 5-8 ft, about a quarter of the spray volume is removed from the pattern by gravity, wind, and air turbulence.[32] But when nozzles are used for close work, as with boom spraying of field crops or the employment of lances for orchard application, the difference is noticeable. Of the two types, the solid-cone nozzles give consistently better coverage and control.[59] Cone nozzles are suitable for emission rates up to 5 gpm, and in the low range they may replace fan nozzles at emissions down to 0.03 gpm.[2]

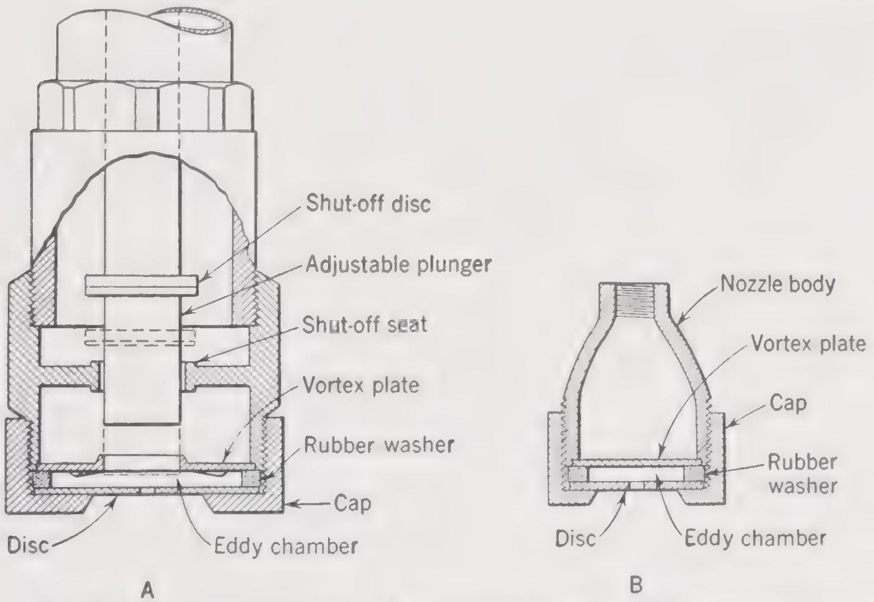

FIG. 7. Eddy-chamber nozzles A. Variable-depth. B. Fixed-depth. (From French, 1942)

In a cone-type nozzle the final orifice is punched through a disc which is secured to the top of the eddy chamber and is replaceable. The specification of the disc is the diameter of the orifice in sixty-fourths of an inch, e.g. a no. 3 disc has an orifice $\frac{3}{64}$ in. in diameter, in North America. Specifications in England

are less uniform, e.g. a no. 3 being $\frac{7}{64}$ in. and no. 2 being $\frac{3}{32}$ in. The diameter of this orifice has no effect on the droplet size. On the contrary, it does affect the emission rate; since this depends on the area of the orifice, and thus is a function of d^2, doubling the diameter has the effect of increasing the emission rate 4 times. As the orifice and the emission are enlarged, the cone becomes wider and more solid, and its carrying power is consequently increased. Cone-type nozzles usually available have included angles between 15° and 70°. Increasing the thickness of the disc itself, thus lengthening the orifice into a channel, will cause the cone to become smaller and the spray coarser. If the orifice is not exactly circular or perpendicular to the disc, the cone of emission becomes lopsided. Abrasive spray suspensions will wear orifices irregularly, destroying the spray pattern; or they may enlarge them to a point out of balance with the vortex openings, causing the spray to become coarse. Discs are therefore made to be replaceable by unscrewing the nozzle cap which holds them to the eddy chamber. There are disc orifices made of exceptionally hard steel which are inset in the nozzle caps (e.g. *Hard-center*). The rate of emission and the regularity of the cone may also be affected, respectively, by the size and regularity of the channels in the vortex plate.[32]

The **Bordeaux nozzle** may be compared to a leaky tap, in which the leak has been utilized to give a spray. The stream is broken by a bevelled internal obstruction which may be adjusted for fine atomization. The liquid emits through a window in the side of the valve seat, giving a fan-shaped spray of considerable volume. A turn of the cone or barrel will substitute a hole right through it, clearing any clogged sediment and giving a high-emission jet. These high-volume delivery nozzles, which were favoured for calyx sprays, are becoming obsolete[1] (Fig. 5).

There are a number of nozzles which are used for special purposes. Oil-burner nozzles are used for field application of liquefied-gas aerosols, since their emission rate is extremely low (2 gph). For emitting a fine stream of concentrated suspension into an air blower, *Whirljet* nozzles are used because they do not clog. Here the liquid enters tangentially from the side of a shallow cylindrical chamber, to whirl around in it before emitting from its end; the spray is thus emitted at right angles to

the feed.[5] Fogjet nozzles such as are used in fire fighting, consisting of a mushroom with a series of slits around the rim, have little application in insect-control work. There are also pneumatic atomizing nozzles into which both the liquid, under pressure up to 40 psi, and the air, up to 60 psi, are introduced, to mix at the nozzle tip.[5]

The atomization of liquids

Atomization is caused by the injection of the liquid into a gas (i.e. air) at high velocity, or the passage of a gas past the liquid at high velocity. The higher the velocity (v) of gas and liquid relative to one another, the smaller the size of droplets. Atomization is increased the greater the volume flow of gas (Q_A) and the smaller the volume flow of liquid (Q_L). It also increases with reduction in the viscosity (μ) and the surface tension (σ) of the liquid. From measurements made with small air-atomizing nozzles, Nukiyama and Tanasawa[8] have been able to equate D_0 (the diameter in microns of the droplet with the same surface volume ratio as the entire spray) with the ratio Q_L/Q_A, with v in metres per second, μ in poises, σ in dynes per centimetre, and with the density ρ. The equation they derived was:

$$D_0 = \frac{585\sqrt{\sigma}}{v\sqrt{\rho}} + 597\left(\frac{\mu}{\sqrt{\sigma\rho}}\right)^{0.45}\left(1000\,\frac{Q_L}{Q_A}\right)^{1.5}$$

Nukiyama and Tanasawa were also able to characterize the range or spread of droplet sizes. A droplet spectrum has the droplets apportioned to each size class in a normal frequency distribution, so that when plotted graphically a normal curve is produced. If the range of droplet sizes is very wide, the frequency curve is broad and shallow; if the droplets are nearly all of the same size, the frequency curve is high and narrow. This frequency distribution may be characterized by the function q in the equation:

$$\frac{dn}{dx} = ax^p e^{-bx^q}$$

where n is the number of droplets in the sample whose diameter is less than x microns, and a, b, and p are constants. The nume-

tion q is a constant for each type of nozzle. For coarse nozzles it is $\frac{1}{8}$ to $\frac{1}{3}$, determining that the frequency distribution of the droplet spectrum is wide. For fine-spray nozzles it is about 1, indicating a narrow droplet spectrum. For very fine nozzles (0.02 in.) at very high pressure (4000 psi), the value of q approaches 2, which is the value for the distribution of molecular velocities in a perfect gas.

The value of D_0 is smaller than the mass median diameter, being generally between one-half and three-quarters of it, depending on the droplet distribution. The relation between D_0 and the m.m.d. may be calculated if the value of q is known.[75]

Effects of hydraulic pressure

An increase in the pressure of the pump has a profound effect on the performance of the nozzles. In the first place, it increases the emission rate, raising it by 20% for every 100-psi increase in pressure.[25] The emission rates of orchard nozzles at pressures from 200 to 600 psi are shown in Table 4. There is a slight variation in the figures quoted by different sources, presumably explicable by particular eddy-chamber characteristics: for example, the gpm for the no. 6 orifice at 300 psi is given as 2.9 in the table based on California figures,[39] but as 2.7 in some figures from Ohio.[4] At 200 psi, the gpm for this orifice is 2.4 in the table, and 2.8 in some figures from Michigan. The increase in

TABLE 4. Emission Rate of Short Spray Gun at Different Pressures

Short-range adjustment[39]

Pressure, psi	Gpm Discharge for the Following Orifice Discs					
	3	4	5	6	7	8
200	0.64	1.10	1.70	2.40	3.33	4.10
300	0.79	1.32	2.06	2.90	4.15	5.05
400	0.91	1.55	2.40	3.40	4.75	5.75
500	1.02	1.72	2.69	3.75	5.30	6.40
600	1.13	1.90	2.94	4.12	5.80	7.00

pressure from 200 up to 800 psi increases the emission from 2.8 up to 5.6 gpm. Changing from the coarse long-range adjustment to fine adjustment reduces the emission rate from 2.8 down to 2.2, and from 5.6 to 5.0 gpm.[25] There is no material difference between the flow rates of oil and of water through orifices, because here the emission is turbulent and the viscosity of the liquid has no part in determining it. However, increasing pressure has a slightly greater power to stimulate the flow rate of oils than that of water, varying as $p^{0.6}$ for SAE 30 lubricating oil as against $p^{0.5}$ for water.[70]

The most significant effect of a rise in pressure is an increase in atomization. The droplets in an orchard spray are a mixture of sizes varying from half a millimetre (500 μ) in diameter down to 1 μ or less; the effect of pressure is to increase the number of droplets in the smaller sizes at the expense of the larger size classes (see Table 5). For example, the average diameter (of

TABLE 5. Droplet Spectra of Oil Spray with Various Nozzles at High and Low Pressure[119]

Type of Nozzle	Pressure, psi	Per Cent of Droplets in Size Range, μ					
		10–40	41–80	81–120	121–160	161–200	201+
Hollow-cone (LNN2)	60	30	35	18	8	6	3
	150	46	38	14	2	..	..
Solid-cone (GG2)	60	1	21	24	21	14	19
	125	19	25	24	12	3	17
Flat-fan (TTL)	60	1	18	19	24	22	16
	125	17	44	20	8	6	5

droplets obtained from an aqueous suspension of slaked lime, which was found to be 380 μ at 200 psi, decreased to 170 μ when the pressure was raised to 1000 psi[39] (see Fig. 8). With the usual orifice size of 0.05–0.125 in. used in hydraulic sprayers, the droplet size varies inversely as the square root of the pres-

sure.[70] For example, by dividing the pressure by 4 (reducing from 800 to 200 psi) the average droplet diameter is multiplied by 2 (increased from 200 to 400 μ). The diameter of the orifice of these eddy-chamber nozzles has no effect on the atomization. With smaller orifices, however, the restriction of the orifice diameter does become a factor in producing fineness of spray, for decreasing the diameter from 0.05 to 0.03 in. decreases the average droplet size at 200 psi from 400 down to 200 μ.[1]

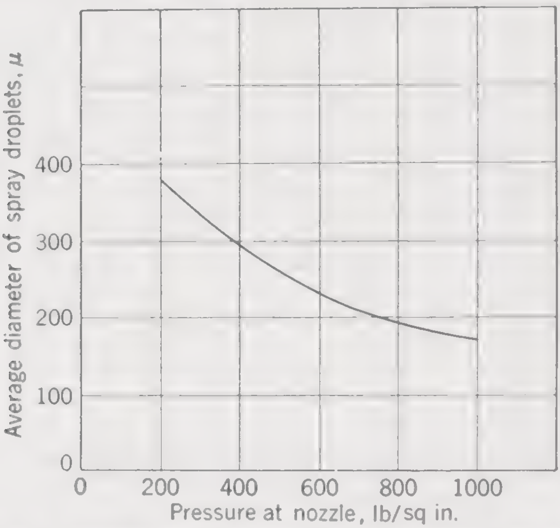

Fig. 8 Effect of pressure on droplet size obtained with a hollow-cone nozzle. (From French, 1942)

Increasing pressure also has the effect of slightly widening the cone of spray. For example, a rise in pressure from 7 psi to 60 psi enlarges the included angle of a hollow-cone spray from 67° to 72°. It also has a tendency to make the cone lopsided, which must be corrected by special design.[32] The fan width of flat-spray nozzles is similarly slightly increased by pressure; a graph has been published showing this relationship. As a consequence mainly of the increase in volume emitted, increasing pressure will lengthen the distance the spray carries, despite the decrease in droplet size. The momentum of so much material creates an air current which carries along the fine droplets. A single-nozzled gun with the fine close-range adjustment will

throw the spray 8 ft at 200 psi, 16 ft at 600 psi, and 17 ft at 1000 psi. With the long-range coarse adjustment the distance of carry is 27 ft at 200 psi, and 34 ft at 600 psi, decreasing to 33 ft at 1000 psi[23] (Fig. 9). The effect of the various factors upon the performance characteristics of nozzles is summarized in Table 6.

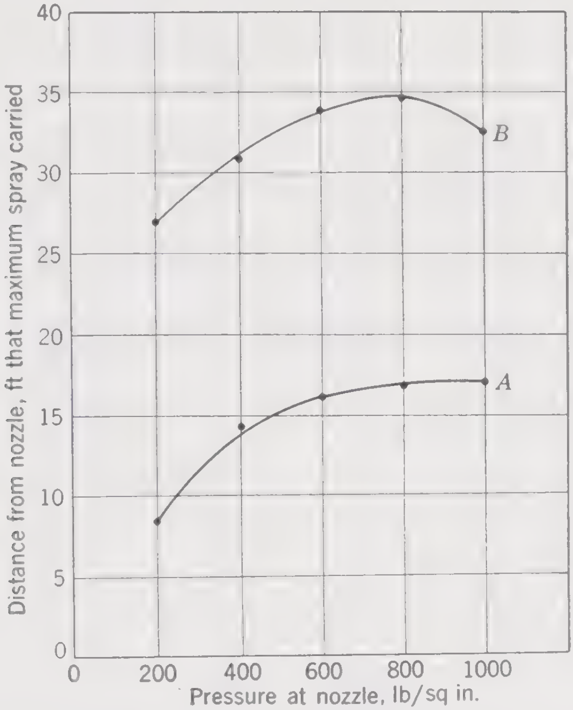

Fig. 9. Effect of pressure on distance the spray carries. A. Short-range adjustment. B. Long-range adjustment. (From French, 1942)

The use of high pressure in orchard work has afforded a great improvement in the coverage of the spray; whereas an application made at 200 psi gave only 70% control of codling moth, the same treatment made at 1000 psi gives 95% control. Such a rise in pressure decreases the time required to spray a tree from 4 min to $2\frac{1}{2}$ min, thus increasing by 60% the speed at which an orchard can be treated. It should also mean a saving in material because of more even coverage; however, in practice it was found that the spray expenditure per tree rose from 9 gal at 200 psi to 15 gal at 500 psi, before decreasing to 12 gal at 800 psi.[24]

TABLE 6. FACTORS AFFECTING PERFORMANCE OF CONE-TYPE NOZZLES [32, 39]

Factor	Pump Pressure	Vortex Openings	Eddy Chamber	Disc Thickness	Orifice Diameter
Faster output	+	+	+		+
Finer droplets	+	−	−	−	No effect
Longer carry	+	+	+		+
Wider cone	+ *	−	−	−	+

Vortex openings: + larger, − smaller.
Eddy chamber: + deeper, − shallower.
Pump pressure: + greater, * but the increase produces a lopsided cone.

Higher pressures require much more expensive pumps and put a far greater strain on hose, nozzles, and other equipment. Since the greatest improvement in droplet size and carry is made in the range below 600 psi (see Figs. 8 and 9), and since the degree of codling-moth control is excellent at moderately high pressures such as 400 psi, the advantage of using extremely high pressures has been questioned. The optimum pressure for derris sprays for warble-fly control was found to be 400 psi; at higher pressures the finer droplets bounced off the hide. For orchard spraying in the United Kingdom, a working pressure of 400 psi is recommended for pump deliveries between 5 and 40 psi. But the real advantage of high pressures is in the speed of emission, which continues to rise linearly. Maximum advantage can be taken of this feature only if the number and size of the orifices used are raised to the maximum capacity of the pump. If, however, too many or too large orifices are put on, the nozzle pressure then drops, and the droplet size and emission consequently deteriorate. In this connection it must be remembered that the actual output at the nozzles is 10–30% less than the rated output of the pump,[104] and that pressure gauges are liable to be inaccurate and show readings that are too high.[3]

Compressed-air sprayers

In this type of equipment the spray liquid is pushed to the nozzle by a body of compressed air. The air pressure is built up by an air pump or compressor, instead of hydraulic pressure

being provided by a liquid pump. Nevertheless the conditions actually obtaining at the nozzle are identical with those for the hydraulic sprayer, and in both cases the pressure is measured in terms of air pressure.

In its simplest form the compressed-air sprayer is a pressure can: the spray liquid is charged through a hole which is then closed with an air valve and compressed air is applied to fill the remaining space. Examples of this type are 6-oz to 1-qt cans, which may be pressurized with air up to 300 psi, taken from bombs which are punctured on insertion, or from air supplies at an automobile service station (e.g. *Sure-Shot Sprayer*). The nozzle is located on the side of the can and is operated by a trigger closure; a fine mist is produced, suitable for space spraying of buildings.[102a] Another modification consists of a 2-qt tank which carries an air pump built into the cup of the filling hole, exactly as in the Coleman gasoline lamp or acetylene blowtorch (e.g. *PCE Perfect Sprayer*). The nozzle, flat spray in type, is at the end of an 8-in. angled extension swivel and is controlled by a trigger. A pressure gauge reading up to 60 psi allows manipulation of the fineness of spray by pumping to 25 psi for coarse, and 45 psi for fine, sprays. This type of sprayer is suitable for control of household insects that inhabit crevices.

The most familiar form of this class of sprayer is the 4-gal **compression sprayer,** sometimes termed the pneumatic sprayer. Consisting of a cylinder approximately 20 in. in height and $7\frac{1}{2}$ in. in diameter, it may be slung over the shoulder (Fig. 10). It is equipped with about 3 ft of hose which terminates in a trigger, rod, and nozzle. It is filled three-quarters full with spray liquid, and air is pumped into the remaining space by means of a vertical $1\frac{3}{4}$ in. × 15 in. air pump. The pressures developed by hand pumping may range up to 60, 80, or even 100 psi; several pumpings are necessary to compensate for the increasing air space as the liquid is discharged. This type of sprayer is suitable for garden use, and it may be fitted with a range of nozzle types and even with small booms (e.g. Hudson, Dobbins, or Kent sprayer). It may carry a pressure gauge, and the trigger may be a squeeze valve on the hose (e.g. Lofstrand sprayer). Compression may be provided by a 10-oz cylinder of CO_2

mounted on the outside of the tank (e.g. Chapin sprayer), which is sufficient to deliver five tankfuls of spray liquid.[102a]

FIG. 10. Back-portable compression or pneumatic sprayer. (Courtesy of H. D. Hudson Mfg. Co.)

The compressed-air principle has been developed for boom sprayers by pressurizing the insecticide tank with a compressor to 80–100 psi. Hydropneumatic-system boom sprayers are operated by such an air push.[2] Aerosols have been produced by compressing nitrogen to 350–1000 psi to propel solutions through a fog nozzle.[11a] Light-weight compressed-air sprayers, consisting of two tanks of equal size, one for the insecticide and one for the air, have been used in hillside orchards.[79] The compressed air

is taken on at a central pumping station at each filling of the insecticide tank.

Hydraulic sprayers

Equipment of this type includes most of the agricultural sprayers, such as the power sprayers for orchard, shade-tree, and livestock application, and the boom sprayers for treatment of field crops. Here the spray liquid is pressurized by means of a hydraulic pump, and the pressure may be stabilized and measured by means of a small by-pass air chamber. Depending upon the pump employed, pressures ranging from 20 to 1000 psi may be imparted to the liquid. Emerging at high velocity, the liquid is atomized by the action of air resistance upon the type of spray pencil induced by the particular structure of the nozzle.

The simplest hydraulic sprayer is the **bucket pump,** which is a plunger pump clamped in a pail, delivering by a hose to a rod and nozzle. The pumps may be single- or double-acting; in the latter case they discharge on both the downward and upward strokes. By vigorous pumping, continuous emission may be obtained at fairly uniform pressures ranging up to 150 psi. In a modification of the bucket pump known as the trombone sprayer, the spray liquid is drawn into the hose and discharged through the nozzle by a plunger and cylinder moved on each other like the action of a trombone (e.g. Hudson).

By the use of a light but powerful diaphragm pump it has been possible to develop the **knapsack sprayer,** which is constructed to fit the back of the operator (Fig. 11). The pump is actuated by a lever carried forward to the operator's hand for up and down arc movement. It is provided with a small air chamber for pressure stabilization, and the pressure reaches 50–80 psi (e.g. Dobbins, Hudson, or Ross). The pump is generally mounted inside the knapsack tank, and its movement actuates an agitator; the liquid in the tank is not under pressure. Alternatively a trombone-type plunger pump may be employed on the hose to give pressures up to 180 psi (e.g. Hudson). Knapsack tanks are made to hold 2–5 gal. They are adapted for the treatment of small truck gardens; and since they are usually fitted with swirl-type nozzles, the coarse sprays they produce are suitable for residual sprays.

Fig. 11. Knapsack sprayer. (Courtesy of H. D. Hudson Mfg. Co.)

The next largest sprayer unit is the **barrel pump,** where the plunger pump is supplied with a lever handle and an arc movement like a well pump, and develops a pressure of 200–300 psi. The rod and nozzle unit is provided with a trigger, and a tank agitator is attached to the pump movement. The barrel, can or drum of 15- to 45-gal capacity is often mounted on a wheelbarrow, in which case a 15-gal tank is added as an air reservoir, and an air-pressure gauge allows control of atomization. The wheelbarrow sprayer is suitable for small fields or orchards.

When the pump is operated by a gasoline or electric motor, the wheelbarrow sprayer becomes a miniature **power sprayer.** Machines of this type have been developed for tanks holding from 15 to 50 gal; the single-cylinder pumps develop pressures of 200–250 psi and discharge rates of $1\frac{1}{2}$–$2\frac{1}{2}$ gpm, and are driven by motors of $\frac{2}{3}$–$1\frac{1}{2}$ hp (e.g. Briggs and Stratton, Lauson). When supplied with larger tanks of 100- to 150-gal capacity, the spray-

ers may be mounted on skids for truck transport and may be fitted as boom sprayers. With double-cylinder pumps driven by 2.3-hp motors these power sprayers will develop pressures of 350 psi and delivery rates of 5 gpm.

Trailer-type power sprayers of 150-gal capacity may be constructed with double-cylinder pumps driven by 4-hp engines or power take-off from the tractor to deliver 7 gpm at 400 psi. The pumps may be driven from the rotation of the wheel axle, giving the so-called traction sprayer. The large power sprayers proper are usually mounted on two-wheeled trailers, of 200- to 600-gal capacity, with triple-cylinder pumps driven by 20- to 45-hp gasoline engines (e.g. Wisconsin, Continental) to develop 15–85 gpm at pressures from 600 to 1000 psi.

The performance of the power sprayer is a consequence of the capacity of the positive-displacement, single-acting, reciprocating plunger pump. This depends on the number of cylinders and their diameter, the length and frequency of the plunger stroke, and the amount of leakage past the valves and plunger packings.[39] The spray liquid leaves the pump under high hydraulic pressure to pass successively through a relief valve and a check valve; this allows the pressure to be controlled and the excess liquid to be by-passed and returned to the spray tank. When the emission is shut off at the nozzles, all the liquid pumped becomes excess and is returned to the tank. It is usually piped to the lower levels of the tank in order to prevent foaming and aid agitation, which is normally performed by a longitudinal shaft fitted with paddles that clear the concave bottom of the tank by $\frac{1}{2}$ in. Pressure is measured by a gauge attached to a small air reservoir connected with the outflow pipe.

Orchard power sprayers

The orchard sprayer is usually mobile and is slowly pulled by a tractor along the rows as the trees are sprayed. Stationary sprayers, where a system of pipe lines is laid out from the machine to reach all parts of the orchard, are occasionally employed; in some cases the pipes may be portable. In the usual mobile sprayer, the liquid is pumped by flexible hose to guns, brooms, or lances manipulated by the spraymen, or to tubular booms held vertical to serve as masts for automatic spraying. The

single gun is a 2-ft rod equipped with a nozzle whose eddy-chamber depth may be adjusted by rotation of the grip of the handle, thus varying the spray from a solid stream to a fine fog; still further rotation will shut the spray off at the nozzle. The disadvantage of the use of guns is that the tree-tops may be reached only with the solid stream and its consequent large droplets. This has been remedied by a multiple-nozzle gun, in which 3–8 nozzles are arranged on a small boom or "broom." Here the mutual reinforcement of the nozzles creates an air movement sufficient to carry even the fine droplets a long distance. Guns and brooms may be handled from platforms on the spray tank (Fig. 12). Alternatively, spray rods or spray lances may be used, consisting of 6-ft to 12-ft lengths of aluminum or brass tubing contained in a bamboo rod, and bearing a pair of nozzles at the tip (e.g. Cooper, Pegler, and Co.). A single-nozzle gun will handle the full output of the pump up to 35 gpm; at higher

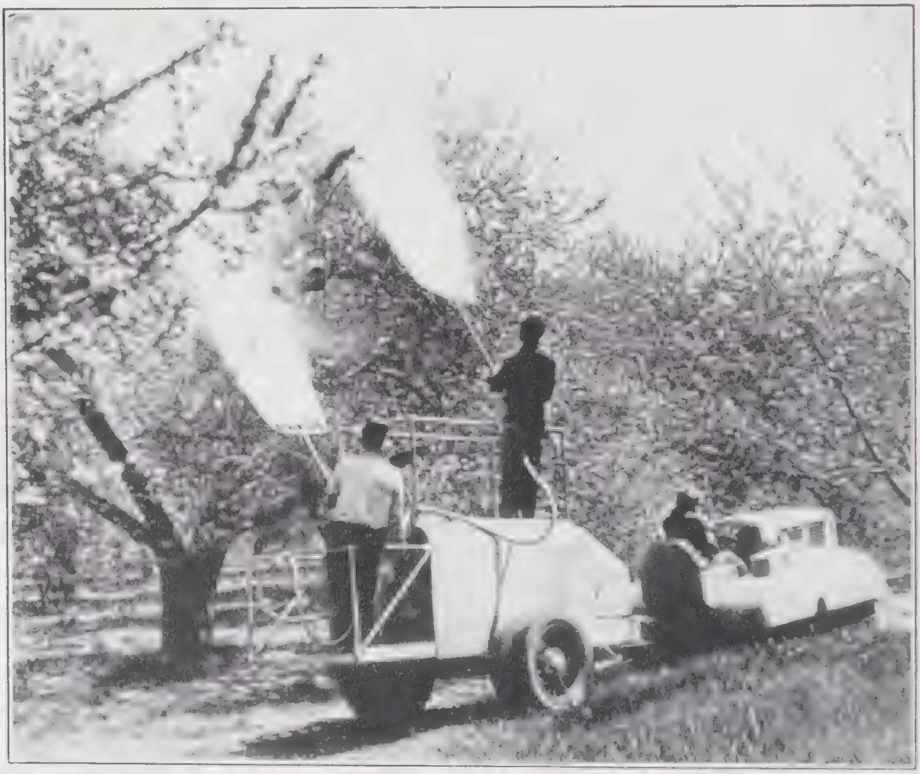

FIG. 12. Power sprayer with multiple-nozzled brooms. (Courtesy of Canadian Industries, Ltd.)

outputs two spraymen with guns should be employed. When brooms are used, they should have 3–4 nozzles if the pump output is 30 gpm or less, and 6–8 nozzles if it is 35 gpm or more.[108] When tall trees are sprayed, the guns and booms may be handled from a platform atop a mobile spray tower.

With sprayers which deliver more than 45 gpm, a spray mast may be used to carry the 4 single guns which are necessary for distance of carry. These masts usually extend 6–8 ft above the tanks and may be double for spraying two rows of trees simultaneously (e.g. *Automast*); they may be laid obliquely at the back of the tank with the guns pointing upwards (e.g. *Lowboy*); or cone-type nozzles may be arranged on a boom describing an outward-facing arc around and above the tank, with a gun at the top end (e.g. *Orchard boom*). Instead, high-delivery nozzles may be grouped into rectangular cases whose direction of aim may be oscillated mechanically from a 45° to a 65° angle and back 50 times a minute (e.g. *Iron Age*). Spray masts and booms may be custom-built for the individual orchard.[91]

A pressure loss occurs in the pipes between pump and nozzle, because of the friction of the liquid with the inside walls; quantitatively it is directly proportional to the length of pipe involved. The loss is especially marked at high delivery rates, since it increases as the square of the delivery rate (Fig. 13). It also increases very markedly as the bore of the hose or pipe is decreased, varying inversely as the diameter raised to the power of 2.8. For example, the pressure loss in a 50-ft length of ½-in. pipe is 250 psi at 20 gpm, as against 40 psi with a ¾-in. pipe, or 65 psi at 10-gpm emission.[108] The longer hose lengths required for ground spraying limit the brooms to 6 nozzles rather than the 8 nozzles employed in tank spraying.[3]

The choice of the size of power sprayer is dictated by the size of the orchard. A large sprayer with a 500-gal tank and an output of over 35 gpm is required if the area exceeds 25 acres or if a single application involves more than 10,000 gal.[94] Power sprayers are not required at all if the volume of the application is less than 500 gal; if it exceeds this figure a 10-gpm sprayer is indicated, while an application of 3000 gal requires 12 gpm, and 6000 gal requires a 15-gpm rate of emission.[3] The gallonage per tree required for a single cover spray is roughly two-thirds

of the age of the tree; if the tree is younger than 10 years, this ratio decreases till it is one-fifth for a 2-year-old tree.[165] The gallonages required for the prepink, pink, and calyx sprays are, respectively, one-quarter, one-third, and one-half the tree's age.[16]

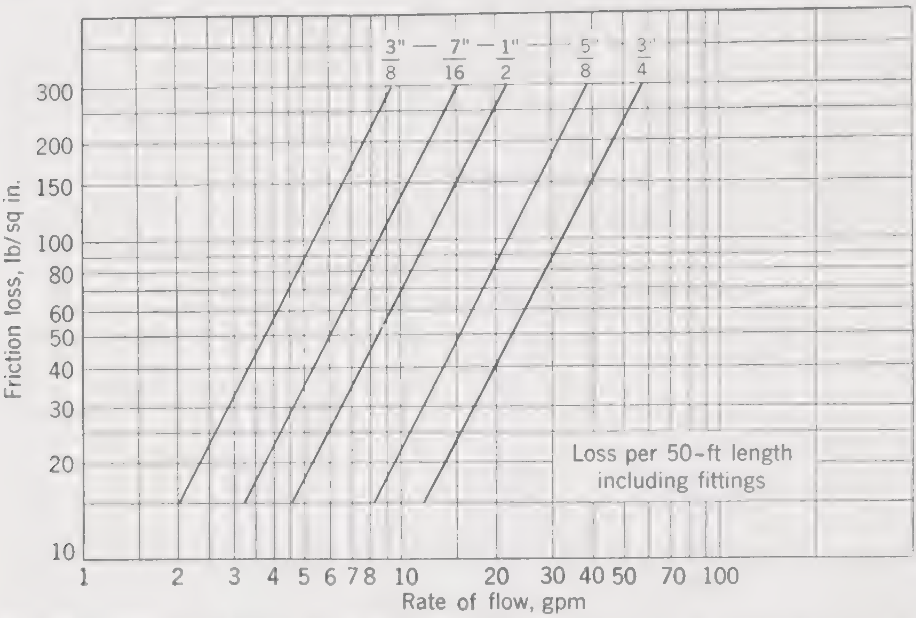

FIG. 13. Friction losses in different sizes of spray hose at various rates of flow. (From French, 1942)

The aim of orchard spraying is to achieve an even coverage on the tree with "a finely broken spray fog." Dormant sprays must cover the twigs and trunk, and postblossom sprays are especially aimed at the calyx cups. Cover sprays not only must reach the fruit sheltered by the leaves, but also must cover the leaf undersurfaces adequately for control of aphids and the young codling-moth larvae. For this purpose, 0.4% suspensions of lead arsenate and 0.1% solutions of nicotine were used formerly. Now 0.05–0.2% suspensions of wettable powders carrying up to 50% of the new organic insecticides are employed. In any case the great bulk of the spray is water. It should be applied as a dense cone of reasonably fine spray driven with sufficient force to reach the target. A thin fog-mist fails to give a deposit of these aqueous sprays, since much of it may evaporate away, and droplets of less than 5 μ diameter have not sufficient momentum to impinge upon the foliage. In practice much of the deposit is

produced by vertical settling of the spray,[26] and the very small droplets are found not to penetrate into the calyx cups.[39] The ideal is to apply the droplets so evenly that their coalescence is postponed until the highest possible deposit has been attained.[24] In normal spraying practice the average percentage of material lost by drip of excess deposit is approximately 10%.[34] It would appear that there is no run-off from the apple until the coalesced drops exceed 5 mm in diameter; when run-off occurs, the elongated areas of residue left thereby are rough enough to prove attractive to the entry of codling-moth larvae. The coverage may be slightly improved with spreaders or stickers,[18] but their addition increases the cost of the application,[3] and they are not really needed if the spray is of correct fineness and has been properly applied.[27]

Fog-drive multiple-nozzle broom guns are the preferred means of obtaining underleaf and tree-centre coverage by men working on the ground.[25] Although single guns can throw a solid stream to the treetops from the ground,[27] they cannot achieve satisfactory underleaf coverage;[3] broom guns can reach the treetops from towers or tank top. The best apparatus for treetop spraying is the lance, which greatly improved the control at 25 ft above ground.[26] Trees over 20 ft high treated with lances showed 90–95% coverage at the lower and middle levels, 65% in the interior of the crown, and 45% coverage at the top.[33]

The single-nozzled gun, whose horizontal range is 25 ft, is preferable on the grounds of speed and ease of manipulation, and for its greater flexibility over different parts of the tree.[27] However, it endangers foliage within 15 ft of the nozzle when the solid stream is used, and even its wide-angled fog adjustment is unsafe within a range of 5 ft.[5] Guns therefore are only for the expert sprayman to handle.[103] On the other hand the fog-drive brooms are safe almost up to the nozzle.[5] But brooms cannot be used in a high wind, which has little effect on the solid-stream gun.[103] This disadvantage can usually be overcome by spraying in the evening and into the night.[25] The clustering of nozzles in a centrosymmetrical arrangement rather than in a boom greatly increases the carry. The triple cluster, with nozzles pointing slightly outwards to prevent narrowing of the spray, has been endorsed by English workers. Clusters have two other advan-

tages over brooms: their traverse width remains the same in whatever way they are swept across the foliage, and they are less liable to catch in branches.[33]

Boom sprayers

Power sprayers may be adapted for the treatment of field crops by fitting a horizontal boom with a series of nozzles across the rear end of the tank. The booms employed range in total length up to 42 ft, the usual figures being about 33 ft for cereal crops on the prairies (Fig. 14), and 20 ft for other crops. The boom consists of a tube, preferably aluminum, bronze, or brass-lined, of 1- to 2-in. diameter. The pressure loss at the boom ends is not great, being only 3 psi for 10 ft of 1-in. tube. The boom is carried 16–24 in. above the ground, a height that is just sufficient for the sprays from individual nozzles to coalesce at the crop level. Although developed primarily for weedicides, these boom sprayers have given very good results on crops such as seed clover and alfalfa, emitting 1 and 2% suspensions and emulsions at a dosage of 15–30 gal/acre.

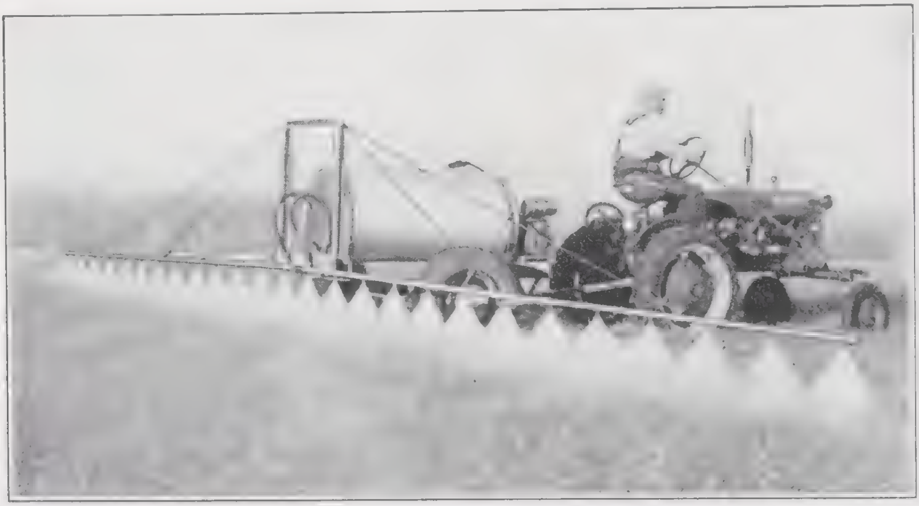

Fig. 14. Boom sprayer suitable for insecticides or weedicides. (Courtesy of F. H. Peavey and Co.)

Solid-cone and hollow-cone nozzles are preferable for insecticide spraying, although the flat-spray nozzles used for weedicides may be employed. In the simplest case, i.e. when they are used to spray low crops, the nozzles are spaced evenly along the boom

at distances such that the fans become contiguous at the ground level. The spacing therefore depends on the height of the boom above ground, and on the included angle of the fan. For a 40° fan, the spacing should be 0.7 times the height, for a 70° fan 1.4 times the height, and for a 100° fan 2.4 times the height. These spacings may be halved to obtain double coverage. The manner in which these ratios are derived may be seen from Fig. 15. Here it may be seen that the 20-in. spacing of two 65°-fan nozzles is too far apart for a spraying height of 12 in. and slightly too close for a spraying height of 18 in.

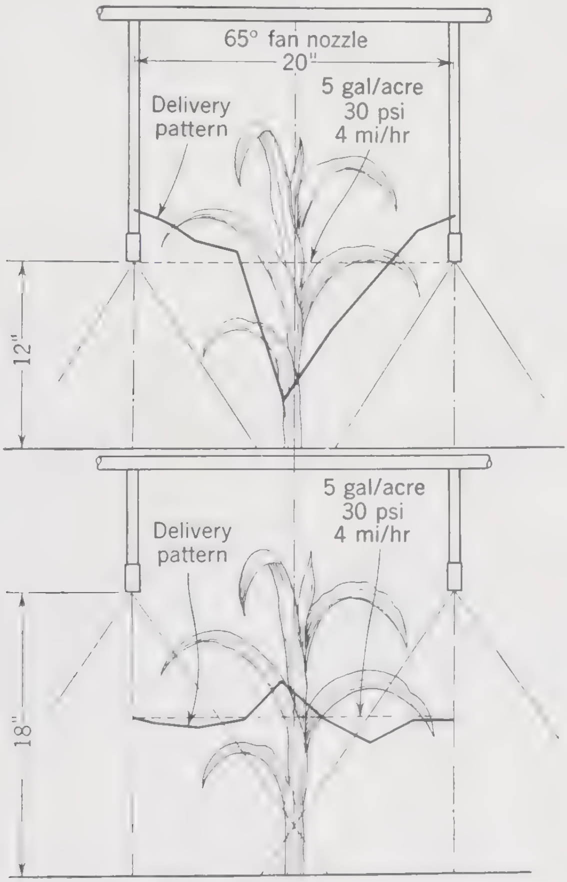

FIG. 15. Relation of nozzle spacing to nozzle height. (From Barger *et al.*)

In many cases the nozzles may be arranged on the boom in pairs pointing away from each other at an angle of 30° with the vertical (Fig. 16). In this way the spacing of boom insets can

be increased to 40 in. The fan from each nozzle just overlaps its mate vertically below, and has a considerable length of overlap with the closest nozzle of the next pair. At an included angle of 60° between each of the pair, these nozzle pairs give satisfactory coverage at this spacing if the fan is 65° and the spraying height 18 in., or with an 80° fan and a 14-in. spraying height.[12] Paired nozzles have recently been developed with the angle as wide as 100°, and the outer or horizontal portion of the fan so reinforced that between them they can cover a width of 100 in. (e.g. *Boomjet* nozzles).

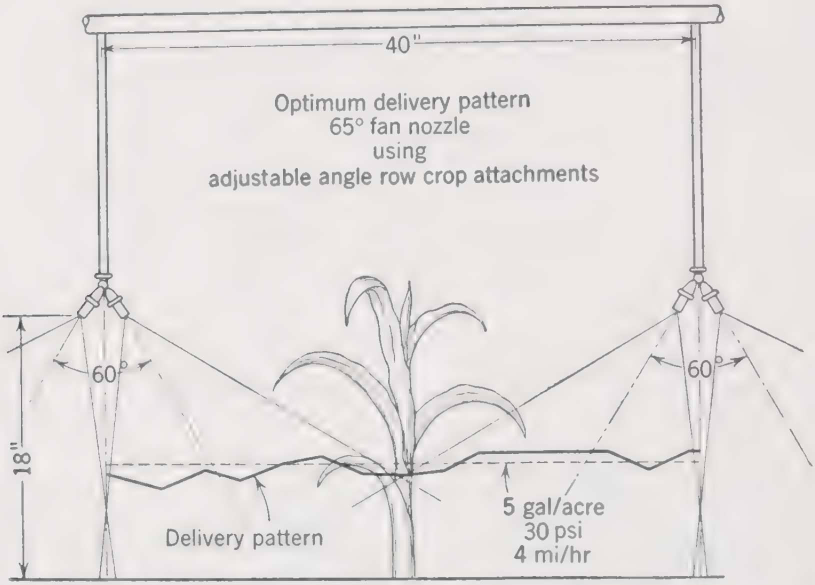

FIG. 16. Increase in spacing of downpipes by using double nozzles. (From Barger *et al.*)

For the spraying of a tall crop planted in rows, such as maize or corn, the boom is fitted with downpipes of various lengths to hold the nozzles (Fig. 17). A single short downpipe may apply the spray from above, while two long downpipes carry nozzles which point into the plants from either side. The nozzles and downpipes may be set directly in the boom, or may be linked on flexible hose to slide along the solid boom to the positions desired. For spraying grapevines, a hooded-boom sprayer has recently been devised (U.S.D.A. Bulletin EC-12). A variant of the boom sprayer is the "whirling sprinkler," in which paired

nozzles are set at the end of a 10-ft boom which is rotated and operated at 200–300 psi, and which can spray an area 20–30 ft in diameter.[2] The alternative is a to-and-fro sweep of a single nozzle, obtained by using the head of an electric washer (e.g. *Wigwag sprayer*).

The boom lines are protected with screens of 100–150 mesh, to prevent their being clogged with coarse particles. Lest the sediment falling to the floor of the boom clog the nozzles, the latter are tapped off the sides; the sediment may periodically be cleaned out by approach from the boom ends. The nozzles also are protected with screens, whose holes are one-quarter the diameter of the orifice. Not only the orifices need to be protected from clogging, but also the spring-loaded valves that ensure sharp shut-off and reopening at 5 psi. Some nozzles are fitted with a plunger pin which allows residues to be cleaned out without dismantling.

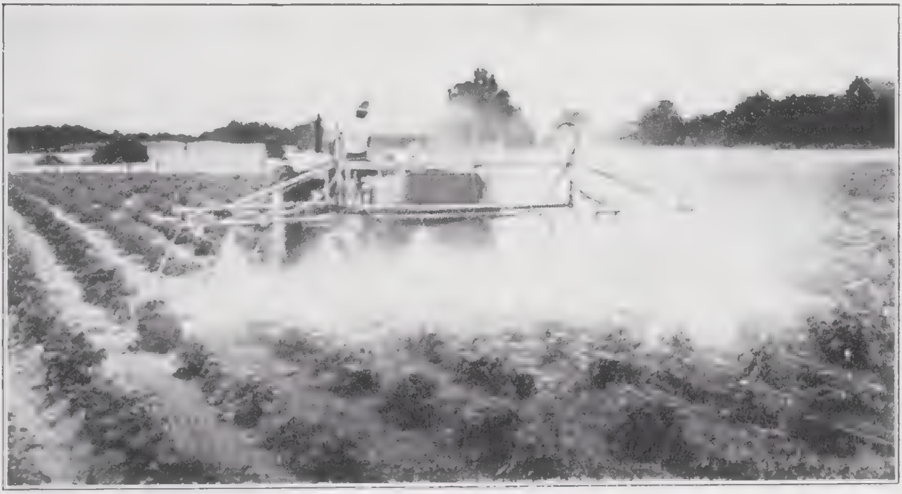

Fig. 17. Boom sprayer with downpipes. (Courtesy of John Bean Division, Food Machinery and Chemical Corp.)

The pump is operated by a gasoline motor or power take-off from the tractor; the principle of utilizing the rotation of the wheel axles, as in traction sprayers, is no longer common. Boom sprayers require less pressure and volume output than orchard sprayers. However, since in many cases they are also used for orchard and cattle spraying, the high-volume plunger pump is often used. Other positive-displacement pumps, the gear pump

and the rotary pump, are satisfactory but are damaged by the abrasives present in suspensions of insecticides. Of the non-positive displacement pumps, the flexible-impeller type is cheap and resistant to abrasion, but its impellers are deteriorated by oil and it does not develop more than 50 psi. The regenerative turbine pump, consisting of a rotor with many small blades, develops a high pressure at a reasonable velocity. The centrifugal pump is the type that is most commonly used; it operates satisfactorily at pressures up to 40 psi, but higher pressures require an extremely high velocity of rotation. However, the volume of liquid required in crop spraying is small in comparison with that needed in orchard spraying, and smaller nozzle orifices are required to accommodate the lower volumes. Since smaller nozzle orifices involve smaller vortex plates, the pressure required to produce a given fineness of spray is much less. Thus the optimum pressure for low-volume water sprays is found to lie in the range of 75–125 psi; and for oil sprays, which shatter more readily and are liable to faster delivery, from 15 to 50 psi. This latter situation brings boom spraying within the range of the centrifugal pump.

It is the area to be treated coupled with the time available, in other words the required speed of treatment, which decides first the boom length, then the size of pump and engine, and then the individual nozzle output. It may be stated as a rule of thumb that when 3 days are available for the application, 1 ft of boom length should be allowed for every 10 acres to be treated. The calculations are as follows: [2]

A. Boom length dictated by

$$\frac{\text{Area to be treated}}{\text{Time available} \times \text{Tractor Speed}} \doteq \frac{\text{sq ft}}{\text{Working hours} \times \text{ft/r}}$$

$$= \frac{43{,}560 \times \text{Acres}}{\text{Working hours} \times 5280 \times \text{mi/hr}}$$

Thus for a 250-acre field to be covered at 5 mi/hr in three 8-hr days (of which 70% is spent in actual spraying) the boom length required is 24 ft.

B. Pump output in gpm $= \text{sq ft/min to be covered} \times \text{gal/sq ft to be applied}$

$$= \text{ft/min} \times \text{boom length} \times \text{gal/sq ft}$$

$$= \frac{5280 \times \text{mi/hr}}{60} \times \text{Boom length} \times \frac{\text{gal/acre}}{43{,}560}$$

Thus for 100 gal/acre maximum dosage to be applied at 5 mi/hr with a 25-ft boom, the required output is 25 gpm (1 gpm for each foot of boom).

$$C.\ \text{Engine horsepower} = \text{gpm} \times \frac{\text{psi}}{1730} \times \frac{1}{\text{Efficiency}}$$

(efficiency being about 0.2 for small units, up to 0.8 for large.)

Thus for 25 gpm and 40 psi, the horsepower required is 2.9.

Then add 25% to the horsepower required to get engine rating.

Therefore a 3.5-hp engine should be installed.

$$D.\ \text{Nozzle output in gpm} = \frac{\text{Pump gpm}}{\text{Number of nozzles}}$$

$$= \text{Pump gpm} \times \frac{\text{Nozzle spacing}}{\text{Boom length}}$$

Or the gpm may be read from equation *B* by substituting nozzle spacing for boom length. (Nozzle spacing is dictated by spraying height and fan width at psi used). Thus for 70°-fan nozzles used at 2-ft height, the spacing is 2.8 ft. For a 25-ft boom, 10 nozzles are required; for 25 gpm, each nozzle should have a 2.5-gpm orifice.

Air atomizers

In sprayers of this type the liquid is aspirated to the nozzle by the passage of a brisk flow of air over the end of a vertical aspirator tube. The air may be moved by an air pump, or may come from a reservoir of compressed air charged by a compressor, or may be impelled by a high-velocity fan. The spray liquid itself is not pressurized, nor is it impelled by a pump; it therefore does not require a pressure-proof container.

The simplest example is the mouth atomizer, which consists of a tube extending horizontally from the mouth to abut on a vertical aspirator tube. Sufficient pressure may be exerted by the human diaphragm to give a coarse spray. When a rubber bulb is substituted as the source of air, the nasal atomizer is obtained; here the air and liquid are generally carried separately in parallel horizontal tubes, to mix at a nozzle. By substituting a piston-type air pump, the familiar **hand sprayer** is obtained (often described as a *Flit-gun*). Each compression stroke of the air piston draws the liquid up the aspirator tube and atomizes it at the top, which is simply cut at right angles. In these opposed-jet atomizers the distance between the air and the liquid jets is critical, and there is a strong tendency to spit. The aspirator tube is

usually about 0.1 in. in diameter; if it is replaced with a 0.017-in. capillary tube, the atomization becomes so fine that the spray compares favourably with a liquefied-gas aerosol.[71] In some hand sprayers the mixture of atomized droplets and air is carried further to a nozzle, whose orifice in some cases may be alternated to give fine or coarse spray. In the continuous-action hand sprayer, as opposed to the simple intermittent type, continuous emission is allowed by a reservoir of air, forward of the plunger and in the tank, which may be compressed by the pump. A trigger may be fitted to its exit, with a device to regulate the volume of discharge of air so that the amount of atomization may be controlled. Some hand atomizers are supplied with a pipe fitting on the pump handle which may be connected to a supply of compressed air.[52] The cylindrical spray tanks, which are usually carried horizontally below the pump, are supplied in sizes from ½ pt to 3 qt [102a] (e.g. Lowell, Hudson, or Dobbins hand sprayer).

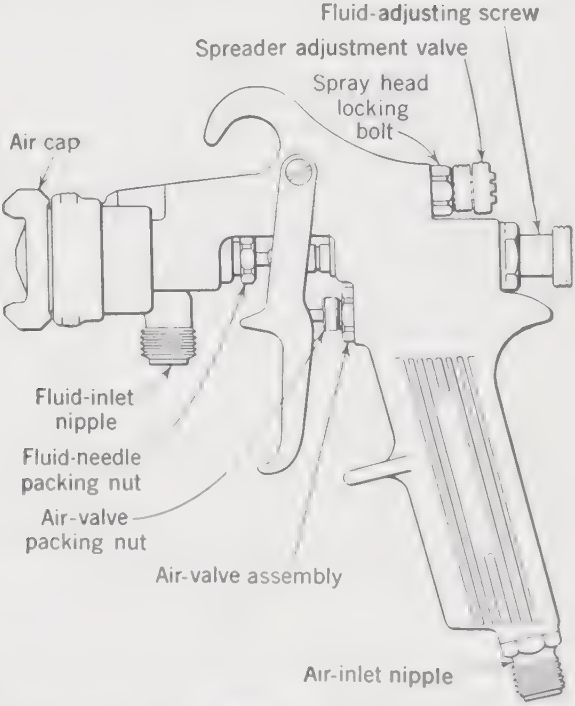

Fig. 18. Paint sprayer, type MBC. (Courtesy of DeVilbiss Mfg. Co.)

Paint sprayers are often used for insect control or insecticide testing (Fig. 18). These atomizers are operated from a supply

of compressed air at 40–60 psi, which they expend at the rate of 5–10 ft^3 min; the air is usually contained in portable tanks of 3- to 10-gal capacity, and they are filled by $\frac{1}{4}$- to $\frac{3}{4}$-hp compressors operated by a gasoline engine or by electricity. When employed in insecticide testing, paint sprayers have been run at pressures of about 20 psi. They give excellent atomization, and the results obtained in fly control in very large rooms are comparable to those given by a liquefied-gas aerosol.[94a] The liquid is brought to the nozzle in a male tube within the female tube which carries the air; the type MBC spray gun is provided with wings from which an air blast may be introduced to flatten the spray fan[112] (Fig. 18).

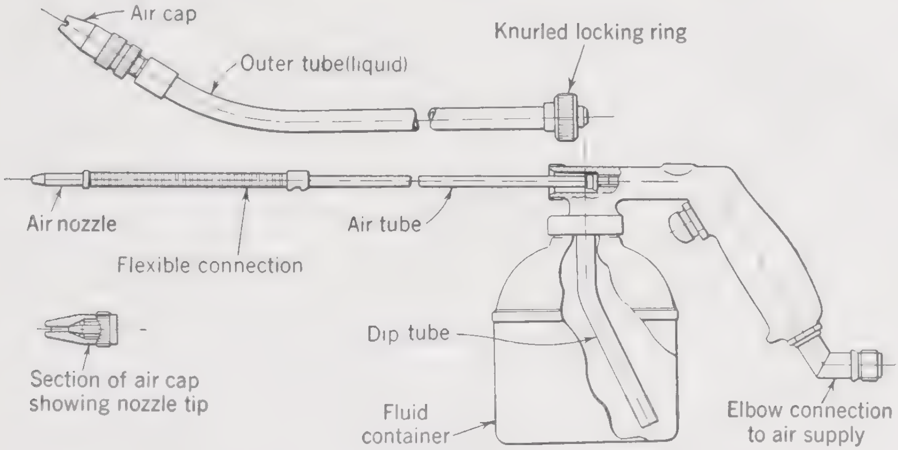

FIG. 19. Oil spray gun or air atomizer. (From Higgins)

Atomizers of this general type (oil-spray guns) have been specially developed for insect control; the air consumption has been reduced to only 1 ft^3 min, which is much more economical than the conventional paint sprayers. These atomizers have a long nozzle and angled tip, fitted with a pistol-grip trigger and carrying the spray container (Fig. 19). The air is emitted along an inner male tube within a larger female tube which carries the spray liquid. The air issuing from the nozzle aspirates and atomizes the spray liquid presented in an annulus around it. The atomization is very thorough and spitting does not occur.[2] In the radiator core gun the liquid is supplied in the male tube, the air in the female; the extension nozzle is straight. These types of atomizers, which produce fine droplets, are especially suitable

for space sprays. When employed in malaria-mosquito control in dwellings where there is no source of electric power, they may be run from a cylinder of compressed air. Large paint-sprayer atomizers have been made which have sufficient power for cattle and orchard spraying; equipped with a $1\frac{1}{2}$-hp engine to operate the compressor, they can deliver air at 150 psi and 1.8 ft^3/min (e.g. *Spraygit Model COWP*). Multiple-nozzled air atomizers shooting spray in all directions are available which may be attached to domestic steam or air-pressure lines or to compressed CO_2 or air cylinders [102a] (e.g. *Fumeral Diffuser*).

The Peet-Grady atomizer (*De Vilbiss no. 5004*), which is standard equipment for fly-spray testing, is a precision instrument constructed on a similar principle to the radiator core gun; it is normally run at 12.5 psi. When it is used to spray a benzene-kerosene (4–1) mixture at 4.4 psi (23 cm Hg) pressure, the droplets are found to range in size from 5 to 90 μ and their mass median diameter is 60 μ.[22] The Peet-Grady atomizer may be adapted for spray-tower assessments of insecticides, by pointing it downwards through a central hole in the lid of the tower; the insecticide solution is dispensed to it by gravity feed from a burette. Since the inner male insecticide tube is apt to drift out of centre with the female air tube, a special atomizer has been devised (*PIL no. AN3*) in which the liquid nozzle may be centred by adjusting screws in the outer cone, and where it may be withdrawn inwards the correct distance by a stem-adjusting nut.[61] Since the spraying pressure is critical, it is measured by a manometer. To avoid the error involved by the increase in pressure when the atomizer is turned on, the pressure is adjusted against an escape valve matched with the atomizer; then spraying is commenced by switching the air to the atomizer with a transfer valve.[61]

In order to eliminate the need for bulky pressure tanks, high-speed rotary compressors have been developed that can keep up to the loss of pressure that occurs during spraying (Fig. 20). These are built into an electric motor, a $\frac{1}{10}$-hp model developing and holding a pressure of 25 psi at the atomizer nozzle. The spray liquid is contained in metal cylinders or glass jars of 1-pt to 3-qt capacity, and may be carried with the motor in a frame or attached to it by flexible air tubing. Its use being confined to buildings supplied with electric power, it is known as the **electric**

sprayer (e.g. Hudson, Piezo). It may also be used as a paint sprayer or insecticide duster. A modification of this type of equipment is known as the mistorizer (e.g. West, Sprayer Corp. of America). Here the spray liquid is atomized directly into the rotary compressor, where the blades beat it up, and then after being warmed a few degrees it is emitted under pressure through a fine nozzle; in this way a fine mist is produced. Like the conventional electric sprayer, mistorizers are fitted with a time switch for 1–30-min emission. A further modification is the fan-type sprayer, in which the air is moved by a blower impeller mounted on the electric motor. The smallest model, with a $1/10$-hp motor, is able to shoot the spray for a distance of 8–10 ft; the largest model, with a $1\frac{1}{3}$-hp motor, can attain 60 ft (e.g. *Mistmaster*). In this latter heavy-duty sprayer, which is nevertheless portable, the mixture of air and spray droplets emerges at a speed of 320 mi/hr and 86 ft^3/min. Thus it has the highest capability to reach inaccessible places with a directed fine spray, which is a characteristic advantage of electric sprayers as a class.[1020]

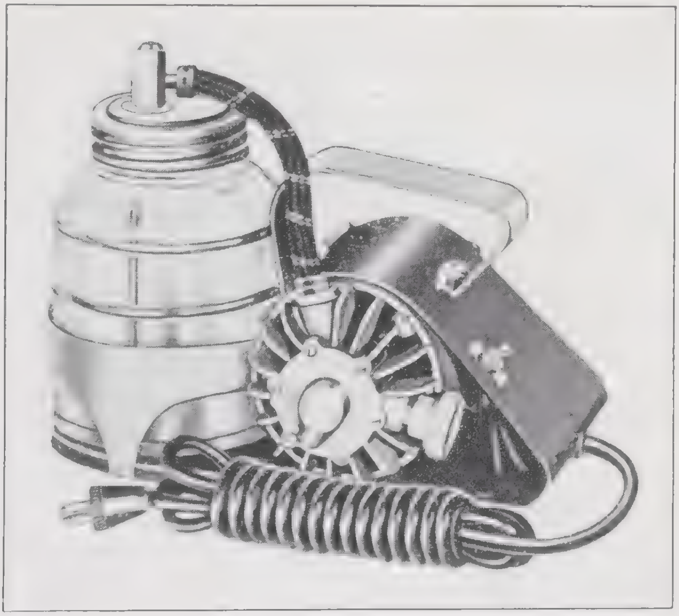

Fig. 20. Electric sprayer. (Courtesy of H. D. Hudson Mfg. Co.)

Air atomizers have been used experimentally in the field for the control of grape leaf hopper in California. Compressed air at

80 psi is emitted through a nozzle abutting at right angles on a second nozzle through which the insecticide solution is drawn by the resultant air suction, in addition to gravity feed. Were the liquid dispensed under pressure, and the air blast more considerable, this equipment would be classed under hydraulic spray blowers (see below). The air provides all the atomization, the average droplet diameters ranging from 35 μ at 80 psi up to 55 μ at 20 psi.[38] Compressed-air atomizers have been found very effective for treating tomatoes three rows at a time.[79] Air-mix nozzles are now available from a few commercial firms (e.g. Hawes-Field-Campbell). Atomizers may even be developed to produce aerosols for greenhouse work, provided the pressure is high enough. Aerosols containing TEPP have been generated with cylinders of compressed air, oxygen, or carbon dioxide at 100–150 psi by atomization into a Venturi nozzle[50] (e.g. *Vapo-diffusion*).

Spray blowers

In this type of equipment the hydraulic atomization of the spray liquid at nozzles or orifices is aided by impelling a body of air past the source of the spray. The air blast serves also to carry the spray to the target, and in this way fine sprays can be aimed. Such machines may equally readily be used for the fine dispersal of dusts ("vapo-dusting"); in fact they were originally developed by modifying dust blowers for the application of liquid concentrates. The arrival of potent insecticides such as DDT, which can be used in 5% solutions or emulsions instead of the 0.5% suspensions of arsenicals, reduced the volume of liquid which required application from 100–1200 gal acre down to a mere 0.5–12 gal acre.[88] For this amount to be applied evenly, a finely atomized spray-mist is necessary; and the air blast is required to carry it to the target. In some spray blowers it is the air blast which is mainly responsible for atomization, as in the turbine sprayer, where the liquid is first emitted from simple orifices. In other types the greater part of the atomization originates at the nozzles and the air blast serves mainly as a carrier for the spray, as in the speed sprayer with its banks of nozzles. None of these machines requires more than 70 psi of hydraulic pressure, since the atomization and carry are aided by

the blower. This allows the heavy plunger pumps to be replaced by light centrifugal pumps, although gear pumps are preferred for the larger machines.

TABLE 7. Types of Mist Blowers Available in North America in 1950

Machine	Tank gal	Motor hp	Blower Type	Muzzle Type	Nozzle Type
Portamist	3	$1\frac{1}{2}$	High-velocity blower	$1\frac{1}{4}$-in. diam. on 3-ft hose	4 capillary jets
Aeromist	26	13	Centrifugal fan	8-in. diam. with baffles	Spray jets
Buffalo turbine	50	18	Turbo supercharger	$10\frac{1}{2}$-in. diam.	Orifices in ring
Rotomist	50	50	Axial-flow fan	24-in. diam. with shear plates	Centre nozzle and 4 peripheral
Speed sprayer	500	85	4-bladed propeller	Radiator-type head	42–150 nozzles
Silveraire sprayer	500	22	Squirrel-cage fan	2 blower cases	Banks of nozzles

Data on several types of mist blowers are presented in Table 7. The first four types have muzzles to conduct and aim the spray-laden air blast, and can reach tree-crowns up to 40 ft in height. The last two emit in an outward and upward direction, and deliver a sufficient volume to attain general coverage without specifically aiming the spray. The rate of emission varies from the 0.6 gpm of the portable mist blower (e.g. *Portamist*), to 4.0 gpm with the turbine sprayer, and 50 gpm with the speed sprayer. The speed sprayers carry nozzles at 70 psi, the portable mist blowers use nozzles at 50 psi or fine 1/8-in. capillary jets at 6 psi, and the turbine sprayer is fitted with 0.04-in. orifices at 20 psi. In the portable mist blower the muzzle is at the end of a 3-ft length of flexible hose. The larger muzzles are made in the shape of pipe angles so that their rotation on the machine changes the direction in which they point; they may have internal baffles to direct the air flow, or shear plates to break up the spray. Muzzles are normally circular but sometimes are flared in the shape of a fishtail. Very large mist blowers have the nozzles tilted on a boom. In the speed sprayer a number of such booms are arranged around the top and sides of a radiator-type spray head. Alternatively, a spraymast may be enclosed in a large oblong case, 8 ft long by 3 ft wide, through which the blower discharges

the blast. In the air-flow type of sprayer, linear banks of nozzles are held in oblong cases which direct the flow of air from the fans (e.g. *Silveraire*).

The blowers fall into two classes: the axial-flow turbine type and the rotary or squirrel-cage type. As an example of the first class, the fan of the turbine sprayer revolves at speeds up to 3800 rpm and can move air at 250 mi/hr through its $10\frac{1}{2}$-in. nozzle. The axial fan of the *Rotomist* sprayer moves air at 165 mi/hr through a 24-in. muzzle. In the second class, the little rotary fan on the *Portamist* machine revolves at 10,000 rpm and moves 120 ft^3/min of air through the $1\frac{1}{4}$-in. muzzle at 240 mi/hr. The squirrel-cage fans on orchard-type mist blowers move up to 20,000 ft^3 of air per minute.[85]

The small portable mist blower delivers a finely atomized spray-mist which has been found to carry for 30 ft vertically and 200 ft horizontally (Fig. 21).[89b] Aqueous suspensions are atomized to show mass median diameters of approximately 50 μ, being roughly equivalent to the output of a hydraulic sprayer at 200-psi pressure. The oil sprays produced by mist blowers are appreciably finer, with mass median diameters of approximately 40 μ.[39]

Fig. 21. Portable mist blower. (Courtesy of John Bean Division, Food Machinery and Chemical Corp.)

The larger mist blowers, which move an 8800-ft^3/min air blast by means of a 25-hp motor, have also been studied. When kerosene was sprayed from the 0.086-in. nozzles at 200 psi into the 120-mi/hr air blast, the mass median diameter of the resulting

spray was 37 μ. When the spray-mist is blown horizontally, there is little sorting of droplet sizes; as much as 100 ft from the blower the mass median diameter was found to be 36 μ as against 42 μ at a distance of 25 ft from it. When the 12-in. muzzle diameter was reduced to 4 in., the air blast had to be increased to 150 mi/hr to produce the same atomization. When aqueous suspensions were substituted for light oil, the droplet size rose from 36 μ to 50 μ; when a wetting agent was added the diameter of the aqueous droplets decreased to 42 μ. An increase in the viscosity of the oil employed from 50 SSU to 200 SSU nearly doubled the resulting droplet diameter.[89a]

Mist blowers of this type, having a high-velocity, low-volume output, have been tested for the application of dormant sprays. They handle 25% emulsions the most efficiently (higher concentrations being too viscous), to replace the 3% emulsions applied by the power sprayers. These concentrated emulsions applied by the mist blower at 2.5 qt/tree have been found to give better control than 50 qt/tree of the dilute emulsions applied by the hydraulic sprayer. The mist blower could achieve a given deposit with one-half to one-third the expenditure of insecticides required by the sprayer, and the same deposit made up of the fine mist droplets was twice as effective as the coarser deposit from the spray. Cover sprays have also been applied as 20% suspensions by the mist blower at a dosage of 3–5 qt/tree, using whirl-jet nozzles to avoid clogging; these wettable powders are emitted at 75- to 100-psi pressure and at a speed of 0.75 gpm. However, it is found that mist blowers exhibit a lack of flexibility in the application of cover sprays, and they are very sensitive to wind, with the result that it is difficult to attain complete coverage.

The turbine sprayer-duster has been used for orchard and shade-tree work, but it has proved to be inferior to a mist sprayer because its air blast is too heavy.[15] The coarser spray it produces makes it more suitable for the control of grasshoppers on field crops (Fig. 22). When an oil (viscosity 7 cp 25° C) spray is emitted through the 0.04-in. orifices at 17-psi pressure into the 250-mi/hr air blast, the mass median diameters range between 110 and 200 μ. When the muzzle is pointed downwind and elevated at 50° from the horizontal, the spray follows a trajectory

that gives the maximum deposit 40–50 yd away; the deposits decreased to one-half of the maximum at 90 yd downwind. The finer droplets are carried much further downwind. When the sprayer is moved crosswind across the upwind edge of a field, satisfactory deposits can be obtained for a depth of 90 yd. in which 85% of the emitted spray is deposited. Mist blowers mounted on high-clearance tractors have been found to allow very fast coverage of corn fields, giving a 50-ft swath in calm air.[67a]

FIG. 22. Turbine sprayer-duster.

The orchard speed sprayers move 20,000 to 125,000 ft^3/min of air at 10 mi/hr by means of a propeller or 36-in. axial-flow fan. The air blast is directed by means of baffles past 42–150 nozzles, each capable of 1-gpm delivery, arranged in four banks around the outer rim of the discharge head.[118] The spray-mist is thrown outwards and upwards with sufficient force to cover the trees on both sides and to reach their tops (Fig. 23). An example of the type of liquid handled by the speed sprayer is a 0.4% DDT emulsion produced by adding 6 gal of an emulsifiable 36% concentration to the 500 gal of water in the tank. Wettable powders may be used in concentrations increasing up to the limit set by clogging of the nozzle system. The nozzle pressure must be high

enough (50–70 psi) for good atomization (e.g. 35–50 μ), and the delivery rate must be fast enough (65–85 gpm) so that good coverage may be obtained as the sprayer is steadily towed along the rows of orchard trees at 0.8–1.5 mi/hr; up to 70 acres/day may be covered by one man driving the tractor[17] (Fig. 28). For this purpose, the lower spreading branches should be cut back to form a hedgerow. The best coverage on both surfaces of the leaves is given when the spray-mist is directed at an angle of 45° with the ground and follows into the tree parallel to the branches. If the spray enters at a shallower angle it catches the upper surfaces of the leaves and blows them into a position which protects the undersurface. When oblong blower cases are used to direct the spray-mist, they should be 8 ft long, with their lower section extending under the lower crown, and the upper section high enough to be able to throw the spray to the top of the tree. For even deposition the spray stream should be directed exactly at right angles to the direction of towing, and the interfering effect of wind should be corrected by shields or dampers. By this means, excellent coverage may be obtained at 1–3 gal/tree in situations where 10 gal/tree was formerly required by the hydraulic power sprayer.[85]

FIG. 23. Speed sprayer. (Courtesy of John Bean Division, Food Machinery and Chemical Corp.)

The shortcoming of all these mist blowers is the danger of incomplete coverage. Applications of spray-mists to citrus orchards at only 10 gal/acre, with the turbine sprayer and Hession aerosol unit emitting chlordane or toxaphene for grasshopper control, showed that only the outside of the tree crowns was covered; although the control was fair to good, it was inferior to that obtained with 10% dusts properly applied.[63] With the speed sprayer it was found that coverage was inadequate if the expenditure was reduced below 325 gal/acre,[16] or below 4 gal/tree. Tall trees in older orchards presented difficulties solved only by top-off sprays applied from a tower on the conventional power sprayer.[55] Foliage injury was also a problem. But nozzles are now available for speed sprayers to deliver regular orchard sprays at one-half the volume and twice the concentration. Complete control of codling moth on pears has been obtained with the speed sprayer, without fruit or foliage injury, at a cost one-eighth of that with the conventional power sprayer. However, for mite control the air-blast sprayer proved superior to the power sprayer only when using fivefold concentrates, and was inferior when emitting at the normal dilution. Present practice in concentrate application is to use 3 to 4 times the normal concentrations recommended for power spraying. The larger mist blowers and speed sprayers are economic for orchard areas exceeding 100 acres.

Aerosol generators

Hot gases. In these machines, oil solutions of insecticides are finely atomized by a blast of heated air or exhaust gases from a gasoline engine. The shatter afforded by the high-velocity blast is enhanced by the heat decreasing the viscosity of the oil. The droplet size is further reduced by the vaporization which occurs before the aerosol is committed to the outside air.

The oil may be injected into the air blast from the sides of the exhaust stack; this arrangement is discussed in Chapter VI under aircraft-exhaust aerosol generators. However, it is preferable to use a coaxial tube for injection, so that the oil pipe is conducted inside the exhaust stack for some distance. When the oil is emitted, fairly close to the exhaust outlet, it has already been heated to a low viscosity. Since the emission orifice is gen-

erally quite large, sufficient injection pressure is developed by gravity feed. Such installations have been made on portable $1\frac{1}{2}$-hp gasoline motors and have been used with success in barns, greenhouses, and warehouses. Here the exhaust is emitted through a $\frac{1}{4}$-in. hole in a pipe cap screwed on to the end of the stack; the $\frac{3}{16}$-in. oil-injection tube is carried up to the hole in the cap, leaving enough room (a little less than $\frac{1}{32}$ in.) for the exhaust gases to escape around it and atomize the oil (Fig. 24). When the oil is supplied by gravity feed at 1 gal/hr this installation atomizes kerosene to an aerosol of 15-μ droplet diameter. If the machine is running at too high a temperature, the normal white aerosol takes on a bluish tinge since the droplets have become too small.[115]

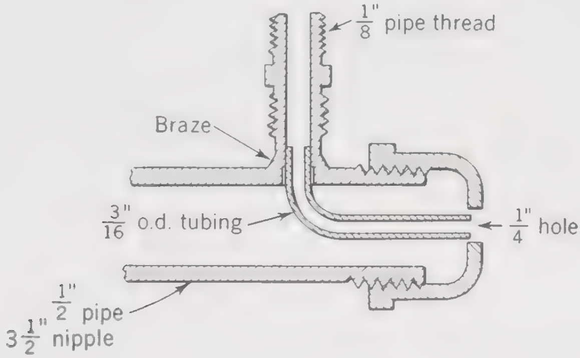

FIG. 24. Exhaust aerosol generator for portable gasoline engine. (From Yeomans and Bodenstein)

A similar atomizing unit has been made to slide over the end of the exhaust pipe of a truck or tractor.[114] Here the end of the injection tube is closed by a $\frac{1}{2}$-in. cap which is pierced with slots in the sides to allow emission. It is centred within a $\frac{3}{4}$-in. pipe nipple, which serves as the orifice and which is attached to the end of the exhaust stack by a pipe adapter. The insecticide solution is delivered at 0.3–2.0 gpm by a gear pump or a pressurized tank, or by gravity feed. Droplet size may be decreased by restricting the insecticide supply, increasing the speed of the engine, or moving the installation closer to the engine.

Exhaust aerosol generators have been installed in the military 5-cwt truck known as the "jeep."[93] They were originally constructed with a narrow throat (on the Venturi principle) similar

to that employed on aircraft. For vehicles in normal use, a coaxial tube 5 in. long by ¼ in. in diameter is constructed to emit into a ⅜-in. throat pipe. With the engine running at 2000–3250 rpm, gas velocities of 800–1500 ft/sec are developed. The insecticide solution (e.g. 20% DDT in *Velsicol*) is delivered by gravity feed at rates from 5 to 50 gph, depending on the droplet size required. If excess solution drips from the Venturi exit, the insecticide delivery is too great; if the cloud of white smoke just breaks away from the Venturi exit, the droplet size has been reduced to 10–15 μ. These aerosols have been found to give excellent control of adult mosquitoes over open marsh in a light wind; to achieve control in dense bush, a heavy wind and a high emission rate are required. By increasing the droplet size, good control of grasshoppers may be achieved. With the engine running at 2400 rpm, a 17% solution of DDT in *Velsicol NR-70* was atomized into droplets between 3 and 45 μ in diameter, while 33% of the material was vaporized. There is now a considerable body of information published on the performance of the various "plumber's nightmares" devised for attachment to the exhaust stacks of vehicles.[28a, 59a, 90a]

Special equipment has been developed in which air is heated and pumped past hydraulic sprayer nozzles. An example is the Todd insecticide fog applicator (TIFA, Fig. 25), where air is delivered at 150 ft³/min by a rotary pump at 1300 rpm. It passes through a combustion chamber heated by burning gasoline to a regulated temperature between 800° and 1200° F; the temperature is selected by adjusting the "fuel pressure" to give the desired gasoline supply. The oil solution of insecticide is sprayed through nozzles into a steel cup, where it is given a whirling motion with a little hot air before it is carried through the combustion chamber and out of the muzzle or foghead by the main blast of hot air. It is delivered by a centrifugal pump of 50-gph capacity, which can develop a pressure of 25 psi but whose "insecticide pressure" may be adjusted as desired. The rate of delivery, which is normally 40 gph, may be governed by a metering valve which thus becomes a "particle-size selector." For example, if the injection rate is increased from 10 gph up to 50 gph, the mass median diameter of the resulting aerosol is increased from 5 μ up to 50 μ.[114] In the TIFA, a 6½-hp motor is

sufficient to run the air pump, fuel pump, and insecticide pump which constitute the moving parts of the equipment.

FIG. 25. Hot-air aerosol generator, e.g. TIFA. (Courtesy of Division of Entomology, Canadian Department of Agriculture)

At a combustion-chamber temperature of approximately 1000° F, much of the oil solvent is volatilized, so that the concentration of insecticide in the droplets of aerosol is higher than in the solution as originally injected. There may be some decomposition of the insecticide at this heat, even DDT showing 35% destruction in oil solution (commercial paraffin) and 50% in oil emulsion.[98] But this loss may be minimized by employing less volatile oils such as lube oil. Using heavy oil as the solvent, a 1.4% solution of pyrethrins was dispersed at the coarsest atomization setting without destruction of their chemical and insecticidal properties.[780] With light oils there may be a danger of explosion in cases where the flash point is below that of kerosene; high-flash oils such as *Sovacide* have been especially developed for this machine. As soon as it is emitted into the open air at the muzzle, the temperature of the fog drops to 120–140° F. When the combustion chamber is held at 850° F, and the insecticide solution is injected at 15 gph, the droplets in the cloud average 20 μ when no. 2 fuel oil is the solvent, and 15 μ when kerosene is the solvent.

The thermal-fog applicator is a very useful weapon for eliminating adult mosquitoes and blackflies, the fog being drifted by the wind across the infested area. Complete kills of mosquitoes have been obtained at distances up to 440 yd downwind of the machine. Almost complete kills of adult *Culex* are obtained on exposure for 5 sec to a fog of 5% DDT in diesel oil emitted at 1 gal/min from a machine 200 ft upwind.[53a] In application it is recommended that the area be traversed at not more than 5 mph at intervals of 100–300 yd.[8] Blackflies may be killed at area dosages as low as 0.5 gal of oil (containing 0.2 lb of DDT) per acre. It is considered that the optimum droplet diameter of aerosols for this purpose in the field is 20 μ, with a range between 10 and 50 μ. Application should be made in the evening, as surface inversion is settling in; for treatment of forested areas an appreciable wind speed is a requisite for penetration. Even slight obstructions such as grass margins have been found to interfere with the evenness and consistency of results.[53a]

This fog applicator has given promising results in orchard and vineyard work; DDT aerosols dispersed from it have controlled grape leaf hopper and citrus thrips.[105] Moreover, there is sufficient force in the air blast issuing from the muzzle to carry the aerosol into the crowns of shade trees. An infestation of *Popillia* in the crowns of deciduous trees has been controlled by fogs generated from a 20% solution of DDT at a dosage of 1 lb/acre. Evidently rather large droplets are required, since 100% kill was obtained with droplets of 40–60 μ at a dosage where droplets of 10- to 20-μ diameter achieved only 40% mortality. For shade-tree application a low wind speed is preferable since it increases the time that the beetles are exposed to the fog.[67] For the treatment of orchards, the fog applicator is unsatisfactory at wind speeds over 10 mi/hr, and the deposit is irregular even under calm conditions.[15]

The thermal-fog generator is flexible enough to be useful for application over field crops. A rapidly settling fog may be produced by increasing the particle size, which is readily effected by decreasing the insecticide pressure or increasing the rate of insecticide delivery. Less heat may be applied to the combustion chamber by reducing the fuel pressure; or the air may be left unheated, in which case the machine can function as a mist blower

and give a 25- to 65-μ spray with a xylene-fuel oil mixture. When the fuel pressure is held at a low level (50 psi), a coarse aerosol may be obtained with a solution of chlordane in *Velsicol AR-50*, which deposits droplets of mass median diameter 30–50 μ up to 100 yd downwind and 20–30 μ for the next 100 yd. When this material was emitted along the upwind boundary of a wheat field 90 yd wide at an expenditure equivalent to 1 lb/acre of chlordane, colorimetric assessment indicated an average of 0.28 lb/acre was deposited, sufficient to give 50% kill of the adult grasshoppers (*Melanoplus mexicanus*) infesting it. The cloud appeared to grow by condensation of the volatilized material during its passage, and the growing droplets "rained" down. If the droplet size setting is not sufficiently increased, or if the application is made while daytime ground convection is still high, the fog will not settle into the crop. This problem has been met in one case by attaching a hood or sheet, measuring approximately 3 ft wide by 20 ft long, to confine the aerosol to the target.[107]

This heat-generated fog has also been employed in the treatment of buildings for disinfestation of bedbugs or clothes moths. In this case a fine aerosol, of 10-μ mean droplet diameter and ranging from 1 to 20 μ, is piped from the foghead into the building through flexible metal hose. The usual dosage is 1 gal of insecticide solution per 50,000 ft^3 of enclosed space. These fine aerosols behave as "dry fog" and do not leave deposits on furniture; thus it is not surprising to find that they are of little value as residual treatments.

A recent type of exhaust generator utilizes a pulse-jet engine combusting gasoline at the rate of 60 explosions per sec (e.g. *Dyna-Fog*). The oil solution of insecticide is introduced into the exhaust pipe near the tail end and is atomized and partially vapourized by the pulsing exhaust gases. It is held in a separate tank under 6 psi pressure tapped from the engine head, and is dispensed to the engine by a metering valve. When a mixture of 1 part *Diol 50* with 5 parts of kerosene is dispersed at 12 gph, it is atomized to give a mass median diameter of 2 μ; when supplied at the maximum rate of 45 gph, the m.m.d. of the droplets in the fog is 22 μ. A certain amount of heat decomposition of DDT occurs,[110] but it is claimed to be less than with other exhaust generators.

Steam. The simplest example of a steam aerosol generator is the vaporizer or diffuser, which is often employed in medicine.[1] A jar of water is heated electrically to steam which atomizes a solution held in another smaller container. The solution is also warmed to a viscosity where it is readily atomized by the shearing action of the steam, to separate into fine droplets of aerosol.

The steam aerosol generator (e.g. U. S. Army C.W.S. Disperser E-12, also termed the Hochberg-LaMer insecticide aerosol generator) is a modification of the Besler screening smoke generator, in which equal quantities of water and oil solution of insecticide are pumped through coils of tubing in a combustion chamber. A $1\frac{1}{2}$-hp gasoline engine supplies fuel (gasoline or fuel oil) to the burner and operates two 20-gph plunger pumps for the water and insecticide. The temperature of the combustion chamber may be controlled at any desired point within the range between 300° and 600° F. When the oil-water mixture in the coils passes through the combustion chamber, the water is converted into steam and exerts a pressure of 60–120 psi. As the mixture issues through $\frac{1}{8}$-in. orifices, the steam exerts a shearing action which breaks up the hot oil into small droplets.

When the temperature of the combustion chamber was set at 600° F, solutions of 20% xylene in lubricating oil produced aerosols whose average droplet diameter was 10 μ. The droplet sizes rose to 15 μ at 500° F, 20 μ at 400° F, and 30 μ at 300° F coil temperature. When solutions of DNOC, BHC, and chlordane in heavy alkylnaphthalene oil were dispersed at a coil temperature of 320° F, a coarser aerosol was produced whose droplets ranged from 40 to 25 μ in mass median diameter, and which settled sufficiently to give even deposits for 50–100 yd downwind. Good control of grasshoppers has been obtained with such aerosols, provided the weather was warm enough for the insects to be active or exposed; since only 5–15% of the material emitted was deposited on the target, rather high expenditures were necessary for effective application.

Good control of adult mosquitoes has been obtained with DDT aerosols of 10-μ diameter produced by this machine. Aerosols consisting of droplets 3–8 μ in diameter, which are just large enough to contact insects, controlled mosquitoes for distances up to 1850 yd in the open and 200 yd in dense forest. Slightly

coarser aerosols containing DDT, emitted at the rate of 0.2–1 oz/yd of frontage, gave complete control of gypsy-moth larvae in hardwood forest for distances of 80–270 yd downwind. The deposits were sufficient to remain repellent and toxic for over 2 weeks. It was found here that adequate penetration of the forest required a steady air movement through it, such as is afforded by air drainage down a hillside, or by a free wind speed in excess of 10 mi/hr; roads have a tendency to divert the cloud to follow along it.[68] In the C.W.S. Disperser E-15 a proportioning valve has been installed for adjusting the proportion of water to oil in smaller ratios, and the coil temperature may be raised to 1800° F to give fine aerosols with heavy fog oils. When DDT is dispersed with a mixture of 4 parts of oil to 1 part of water, about 12% of the insecticide content is decomposed at 700° F, but only 0.5% is destroyed at a temperature of 400° F.[43]

FIG. 26. Steam aerosol generator. (Courtesy of Besler Corp.)

A recent modification of the steam aerosol generator involves withholding the insecticide solution from passage through the combustion chamber; instead it is atomized into the steam coil as it leaves the chamber (e.g. the *Bes-Kil* generator). In this way

the decomposition of the insecticide by heat may be avoided. The output of water and insecticide is greatly increased in these machines, being 80 and 120 gpm, respectively. Since the oil is not preheated, the atomization is considerably less for a given coil temperature than in the original machine. With a solution of 40% xylene in lubricating oil, a coil temperature of 600° F gives an aerosol of 40-μ mean diameter, while a temperature of 300° F results in a spray of 100-μ mass median diameter. To obtain a 20-μ aerosol, the coil temperature must be increased to 800° F.[113] The coil temperatures now employed range up to 1000° F, and the steam pressures to 300 psi. Excellent results have been obtained with these machines in the treatment of orchards with insecticides and fungicides in the Pacific Northwest and British Columbia (Fig. 26); as little as one-sixteenth of the volume required by high-pressure spraying is now necessary. Application of a 5% DDT oil solution as an aerosol by this machine gave very satisfactory control of codling moth on pears at a cost slightly less than half that with power spraying.[41] Steam aerosol generators are also highly effective for mosquito control, being capable of treating 150 acres/hr.

A steam aerosol generator of portable size has been made for use in the greenhouse (e.g. the Torpedo aerosol sprayer). Ellipsoid in shape, and measuring 12 by 18 in., it dispenses 40 oz of water and 32 oz of insecticide in 40 min, a volume sufficient to treat 1,600,000 ft^3.[102a] The coils are heated to 375° F by electricity, and the aerosol mixture is emitted at 60 psi, after being specially heated for the last 8 in. behind the nozzle to dry off the steam. The Torpedo sprayer has been employed to disperse 7% parathion solutions in refined oil for the treatment of greenhouse plants.

Since one of the disadvantages of aerosols for orchard work is that they cannot be aimed to travel with their own momentum, an air blower may be installed to carry them in a blast of air. For penetration into the tree crown from below, a fishtail muzzle has been constructed to measure 4 ft long by 2 in. wide, and the air blast is provided by a turbine fan run from a 20-hp engine. When this equipment is towed at 1.5 mi/hr along the rows of trees, it will cover 2 acres/hr.[72] Since this machine is a combina-

tion of aerosol generator and spray blower, it has been dubbed a "hybrid sprayer."

Rotating discs. These aerosol machines consist of a sheaf of thin metal discs mounted together on a shaft, so that they are almost contiguous at the periphery (e.g. Hession microsol). The insecticide solution is brought by way of the hollow shaft into the narrow spaces between the discs. When the sheaf is rotated at high velocity by an electric motor, the solution is forced outwards through the very narrow peripheral spaces by centrifugal force, and is atomized as it is thrown off into the air. The same principle is utilized in the spinner disc employed in aerial spraying. A large field model is available which consists of 21 discs each 8 in. in diameter; it is rotated at 6500 rpm by a 6½-hp motor. When mounted on high-clearance tractors, these discs have given outstanding control of Japanese beetle on corn.[57a] The solution is emitted at 4.5 gpm and is directed to the target by an air blower operating at 4500 cu ft/min. Smaller models are available for the treatment of buildings. Since it does not involve hot gases or steam, this type of equipment is favoured for the production of aerosols of pyrethrum.

The principles of disc atomization have been investigated by pipetting liquids onto rotating horizontal discs; the droplet sizes which are thrown off are remarkably uniform.[106] Droplets of 200-μ diameter are obtained with an 8-in. disc rotating at 3000 rpm, indicating that the atomization is not as great as when several discs are juxtaposed. Finer droplets require very high rotational speeds such as may be obtained with an air-driven spinning top: 18-μ droplets are obtained with a 3-in. disc spinning at 90,000 rpm. It has been found that the droplet diameter (d) produced varies inversely as the angular velocity (ω) and inversely as the square root of the disc diameter (D). Greater surface tension (T) increases size, and greater density (ρ) decreases it. The generalized relationship is $d = \dfrac{3.8}{\omega}\sqrt{\dfrac{T}{D\rho}}$.

Vaporizing and recondensation. Aerosols may be produced by completely vaporizing a solution of insecticide and allowing it to condense in free air. But normally there are too many nuclei for condensation present in the air to allow individual

droplets to achieve any size. Also it is necessary that the solvent and insecticide have similar vapour pressures, for otherwise they will condense at different rates. Aerosols or "fumes" produced by vaporization from a hot plate have not given very good results.[100] Aerosols produced by passing an oil solution through tubular coils in a combustion chamber (as in the Besler M2 smoke generator) have been found to be much too fine to impinge on the bodies of insects. An apparatus has been developed whereby homogeneous aerosols of any desired droplet size may be made from a DDT solution in a lubricating oil of similar vapour pressure; the air is kept free of dust and condensation nuclei are produced as desired by heating sodium chloride on nichrome wire.[65]

Explosive bombs. The dispersal of insecticides by explosive charges in bombs or grenades has been tested against locusts and other insects and found to be unsatisfactory and wasteful. However, a 9-in. cardboard mortar has been developed to puff 10% DDT dusts into tree crowns for control of elm leaf beetle and other shade-tree insects.[42]

Liquefied gas aerosols. These aerosols are produced by the extremely rapid volatilization of a compressed and liquefied gas, to which has been added a 10–20% proportion of a non-volatile oil solution of an insecticide. As the liquefied gas volatilizes, it leaves the oil solution in the form of an aerosol of very fine droplets. The gases used are dichlorodifluoromethane ("Freon") and methyl chloride, the former gas involving no inhalation hazard to warm-blooded animals. The aerosol formulations are put up in thick-walled canisters or bombs, which have been filled to a standard weight by evacuating them and then connecting them to a cylinder of "Freon" 12 compressed under a pressure of 80 psi. The smaller bombs have been replaced by thin-walled cylindrical canisters (similar to beer cans) containing "Freon" 11 or 12 at a pressure of 25 psi. The usual sizes of containers are 1-lb and 5-lb bombs for use in tents, buildings, and aircraft; and 145-lb cylinders for industrial use. The 5-lb bomb may be fitted with a nozzle 1 ft in length, to serve both as an atomizer and a flowrator (e.g. *Lethalaire*). For greenhouse work a 10-lb bomb has been fitted with a movable 2-ft rod and nozzle. For field-crop

work on peas, potatoes, etc., an 80-lb tank may be connected with a 24-ft boom carrying fine oil-burner nozzles.[44]

The formulae first employed for the treatment of dwellings were pyrethrum in sesame oil and or DDT in cyclohexanone solvent, with "Freon" as the propellent. These solvents are now replaced by heavy petroleum oils, such as lube oil, *APS 202*, and *Velsicol* solvents.[71] For greenhouse work, "Freon" is replaced as the propellent by methyl chloride, which is cheaper and more easily compressed; it must not be dispensed without a respirator, but since the insecticide employed is either HETP or parathion, this protection is demanded in any case.[96] For field work, a mixture of acetone and methyl chloride in equal parts is generally employed as the propellent. For single application to rooms, soda-siphon cartridges ("sparklets") are available, which contain 7 gm of DDT-pyrethrum in kerosene-acetone to which 2 gm of CO_2 has been added as a propellent.[77]

In the domestic aerosol bombs and canisters the nozzle is a simple orifice 0.01–0.02 in. in diameter which allows a delivery rate quoted as 1 gm sec. It is located either at the end of a 4-in. length of capillary tubing or in the side wall of a vertical screw-valve. In either case the propellent, in its climb up the tube to the nozzle, decompresses sufficiently to cause bubbles of vapour to form. These rapidly expanding bubbles, along with the subsequent encounter with air resistance, are the agents which cause atomization.[45] The omission of this lead-up tube, even if it is replaced by a cloth or metal screen to increase turbulence in the propellent before it reaches the nozzle, results in much coarser aerosols.[46]

The degree of initial atomization is a function of the pressure of the dispenser and the type of nozzle; the final size of the droplets at the time they remain airborne is a function of the percentage of non-volatile solvent that remains. For example, when the concentration of the solvent (in this case sesame oil) was only 4%, droplets were produced whose mass median diameter was only 2.5 μ; whereas an oil concentration of 16% gave a droplet m.m.d. of 6.5 μ. With dibutyl phthalate as the solvent, 14-μ droplets resulted from a 30% concentration, as against droplets of 1 μ or less for a 10% concentration.[36] In consequence, the optimum concentration of non-volatile material in the high-pressure

aerosols is between 15 and 20%, since it results in m.m.d. values between 3 and 10 μ, which in turn give the highest kills of houseflies. For the low-pressure aerosols, the optimum concentrations fall between 10 and 15%.[81]

DDT-"Freon" aerosol bombs containing DDT and pyrethrum have shown no loss in activity after storage for 5 years. There may be some corrosion of the container due to the production of hydrogen chloride by decomposition of the DDT, but this may be inhibited by including 0.1% propylene oxide in the formulation.[117] The substitution of lindane for DDT eliminates the problem of container corrosion.[35]

Insecticidal smokes

In this category, the insecticide is mixed with some slow-burning material, which is ignited and burned. Incense is a simple example; insecticidal joss sticks have been made by dipping one end in plant gums containing camphor or pyrethrum, although they act mainly as a repellent. The particles in insecticidal smokes of pyrethrum, rotenone, or arsenicals range between 0.3 and 2 μ in diameter.[59] Slow-burning powders have been marketed containing nicotine (e.g. *Nico-fume*) or azobenzene (e.g. *Benz-fume*) for treatment of greenhouses, the former for control of aphids and the latter against mites. These powders, which probably contain a mixture of potassium nitrate with a slowly combustible material such as ground tobacco stems, may be burnt in loose piles or in ½-lb canisters. Or the insecticide has been impregnated on slow-burning papers. One pound of azobenzene is sufficient to treat 10,000 ft³ of enclosed space. It has been found that azobenzene smokes are deposited on surfaces in the form of minute droplets which are stable at 20° C although their setting point is 68° C. This condition of supercooling is known as metastability; only the largest droplets eventually crystallize, the smaller ones evaporating first.[95]

Slow-burning pellets may be made by compressing a mixture of granular cordite and insecticide with kieselguhr as a coolant. Or powders may be compounded of 58–60% of an insecticide such as DDT or BHC, 30–40% of a burning mixture containing sucrose and potassium chlorate in equal proportions, and 2–10% of a coolant such as kieselguhr, diatomaceous earth, MgO, or

$MgCO_3$. If a pound of this material is placed in a canister and lit by a fuse, it will produce smoke for 3 min; it is sufficient to treat 15,000 ft^3 of enclosed space. Two-ounce canisters, consisting of a fuse, a starting mixture, and the burning mixture, have been developed for greenhouse and domestic use; they are fitted with cooling baffles to prevent their igniting completely (e.g. *Murfume*).[9] Another type consists of lengths of $\frac{1}{8}$-in. fabric cord, impregnated with the insecticidal burning mixture, which are put up in canisters.[87]

When DDT or BHC is burned in smoke canisters, there is a loss by decomposition amounting to approximately 30%. In the case of DDT, this is attributed to dehydrochlorination by heat; the loss is increased by ferric iron and may be inhibited by the addition of certain chemicals such as picolinic acid.[17] The recovery of DDT in the smoke may be increased by using more highly purified DDT (i.e. of higher melting point) or by raising the amount of sucrose in the burning mixture.[14]

DDT smokes are deposited as supercooled droplets, which readily crystallize upon being lightly brushed.[24] Deposits of lindane rapidly become crystalline and appear as dendritic growths. DDT smokes achieve adequate control of household insects, but they are capable of only slight penetration into crevices.[102] For housefly control, DDT smokes give up to 80% reduction in population; to achieve results equivalent to those obtained with DDT in wall spray, about 8 times the dosage must be applied in the smokes.[24] At present, the odour of BHC smokes renders them unsuitable for domestic application.

The results obtained with smokes in the field have been even less satisfactory. Smoke clouds of DNOC, although lethal to the migratory locust at a *Ct* of 250 mg-min/m^3, proved quite inadequate in the field. BHC smokes have given better results, giving toxic deposits where DDT does not. Batteries of 1-lb canisters have been able to kill tsetse-fly (*Glossina*) 60 yd deep in the bush and have given 80–90% control at a dosage of 1 oz/acre of the gamma isomer.[53] Nevertheless, 15-lb canisters at this dosage had little effect on *Aedes* mosquitoes in the Canadian forest. Although BHC smokes are lethal to adults of the wheat-stem sawfly (*Cephus*), in practice the cloud does not penetrate into the wheat crop, and the population reduction remained less

than 70% and was sometimes negligible. BHC smokes proved ineffective to kill flying or settled locusts.

A new method of generating fine aerosols involves the use of live steam produced by thermal decomposition of certain chemicals. Organic thiocyanates as well as chlorinated hydrocarbons may be dispersed in this way from 1-lb canisters with little destruction of the insecticide.[34a]

Fumigation

Fumigating equipment is comparatively simple. Dwellings and warehouses were originally treated with hydrogen cyanide by dropping sodium cyanide into 50% sulphuric acid in earthenware crocks. For every 1000 ft^3 to be fumigated, 1 lb of NaCN was dropped into 1 gal of the H_2SO_4 solution. Greenhouses were treated by sprinkling formulations of calcium cyanide (e.g. *Cyanogas*) in dust, flake, or granule form on the floor, at the rate of $\frac{1}{4}$–$\frac{1}{3}$ oz/1000 ft^3. The atmospheric moisture hydrolyses the calcium cyanide, liberating the HCN, which volatilizes. The fumigation of greenhouse plants is performed at night, when the temperature is between 75° and 55° F, and the plants should not have been watered; exposure is limited to 1 hr, after which the greenhouse is ventilated. For domestic use the most convenient form is HCN adsorbed onto cellulosic material and pressed into discoids, which liberate the vapour gradually and can be removed harmlessly when fumigation is complete.

Cyanide fumigation may be performed on vines or on citrus trees in the field. The trees are enclosed in tents of 8-oz duck fabric, which carry markings to measure the volume enclosed. Then $Ca(CN)_2$ is dusted into the tent, or liquid HCN is sprayed into it from a miniature pressure sprayer equipped with a $2\frac{1}{2}$-gal tank, accurate delivery gauge, pump, and nozzle. Fumigation is performed at night when the temperature is between 75° and 50° F, and exposure is for 1 hr; on the average 6 trees may be treated per night.[73]

The more volatile fumigants (methyl bromide, ethylene dichloride, etc.), which are employed to control stored-products insects, are applied from cylinders in which the gas has been compressed into a liquid at pressures up to 25 psi. The gas may be conducted through a piping system into all parts of ware-

houses or flour mills. For treating bulk grain stores, injection lances may be used to introduce the fumigant deep into the material. When fractional doses of fumigants are applied from cylinders, they are fitted with graduated glass applicators ranging in size from 100 cc to 5 lb, to measure off the liquid fumigant which flows in through a standpipe. Methyl bromide may be handled in 1-lb cans; they are punctured by an auger attached to gasketed tubing which is used to carry the gas to the spots that it is desired to treat. Fumigation of this type is generally carried out where the products are at the time—warehouse, railroad car, or ship's hold—all leaks being sealed and checked with the halide leak detector. Special materials such as nursery stock may be fumigated in steel tanks equipped with a gasketed autoclave-type door and appropriate valves and graduates for precise measurement of the fumigant. The provision of an exhaust pump, pressure gauge, and manometer allows vacuum fumigation to be practised at pressure reductions of 28 in. Hg.[11]

Greenhouse fumigation may be carried out by painting a low-vapour-pressure compound such as nicotine or azobenzene on cool steam pipes, and then turning on the steam. Field fumigation may be practised for the control of aphids by injecting liquid nicotine alkaloid into the exhaust from a two-stroke engine; the resulting vapour is momentarily held in the crop by a drag sheet measuring approximately 5 by 18 ft.[109]

Soil fumigation

Soil fumigators are designed to inject fumigants into the soil to a depth of 3–8 in., at points or in lines 12–18 in. apart. The simplest equipment, namely the hand injector, is a syringe of 1-gal capacity which may be adjusted to deliver 1–15 cc of liquid fumigation per point. Larger syringes may be mounted on a wheelbarrow and driven by traction or a gasoline engine (e.g. *Larvajector*).

For field application, trailer applicators are employed which are equipped with a series of 6 or 7 injector teeth or drills, arranged 12–15 in. apart on a heavy boom. They act as soil chisels, and on their rear edge they carry an injection tube to which the liquid fumigant (such as EDB or D-D) is conducted

at a pressure of 10–15 psi, impelled by a small motor and pump. They are followed by a series of packing wheels or a heavy drag-bar which serves to compact the soil. As a simple alternative, fumigants may be sprayed into the soil as it is cultivated (both ploughed and harrowed) by the rototiller.[80] Solid fumigants may be introduced into the soil by a seed drill, or they may be applied along with the fertilizer. Liquid fumigants may be trickled by gravity feed into the furrow ahead of the ploughshare. In this simple method of application it has been found that when a 16-in. plough bottom is used at a speed of 2 mi/hr, a dispensing rate of 14 oz/min is equivalent to a dosage of 16 gal/acre.[62]

Dusters

All dusting appliances operate on the principle of emitting a blast of air in which the dust particles are airborne. In the **hand dusters** the air is pumped by a plunger. The dust container may be located below the plunger tube, or may be an enlargement at its end, or may be the plunger tube itself. The compression stroke of the piston expels a blast of dust-laden air. In some hand dusters a double plunger tube provides a continuous supply of air on both the forward and return strokes.[74] The emission orifice may be provided with an extension tip and flared fishtail nozzle. Capacities of hand dusters range from 1 pt to 2 qt. A simple duster is afforded by a 1 lb carton consisting of two tubes telescoped together; by means of a two-valve system, air is taken in at one end as the carton is lengthened, and emitted from the other end when the two tubes are pressed together, carrying a dust cloud with it. Hand dusters have been constructed by mounting the dust container above a tube through which air is blown by bellows.

A useful type of hand duster for indoor work consists of a swirl-type dust cup with a horizontal extension nozzle provided with a pistol grip and trigger; it is operated by a supply of compressed air from a paint-sprayer outfit.

Knapsack dusters, of 5- to 10-lb capacity, may be operated by a bellows on the top of the cylindrical dust container. A hand lever operates the bellows and agitates screens to allow the dust to flow into a hose and rod tipped with a sieve-type nozzle. The usual knapsack dusters, however, are actuated by a rotary fan

(Fig. 27). Hand cranking revolves the fan and positively feeds the dust in the container to the outgoing air; it may also provide agitation. Either the dust is fed directly into the fan case from the side, so as to reach the fan blades at a point between the centre and the circumference; or it is fed first into an air chamber which is a "vestibule" of the fan, before passing the fan itself to reach the delivery tube. The rotary type of duster, in which the dust is fed on to the fan blades, gives the best performance.[60] The tube terminates in a fishtail nozzle, and it is preferably long enough to reach the ground at a comfortable distance ahead of the operator.

Fig. 27. Rotary-type knapsack duster. (Courtesy of Brown-Manly Plow Co.)

Dusters of similar principle but of larger size may be mounted on a wheelbarrow, and power may be supplied for the fan from the traction of the wheel, sufficient to operate two or four dust nozzles. Power from a light gasoline engine may supply four nozzles on a short boom. Larger dusters may be mounted on a trailer, with traction drive for the fan, and a six-nozzled boom may be used. When actuated by a gasoline engine, the **power duster** may have a 25-ft boom with a formidable array of eight to eighteen nozzles with their delivery pipes. The fan is run at a speed of 3000 rpm or more. The delivery manifold or dis-

tributor head, from which lines radiate to the nozzles, may be of the truncated cone, fishtail, or peripheral type. Nozzles may be V-shaped (with the rear side open or closed), or spoon-shaped for reaching the undersurfaces of foliage (Fig. 28). They are placed at a level as close to the crop as possible in order to minimize drift of the dust. A cloth canopy or structural hood may be attached to the boom to reduce the amount lost by drift; these installations are, however, never completely effective.

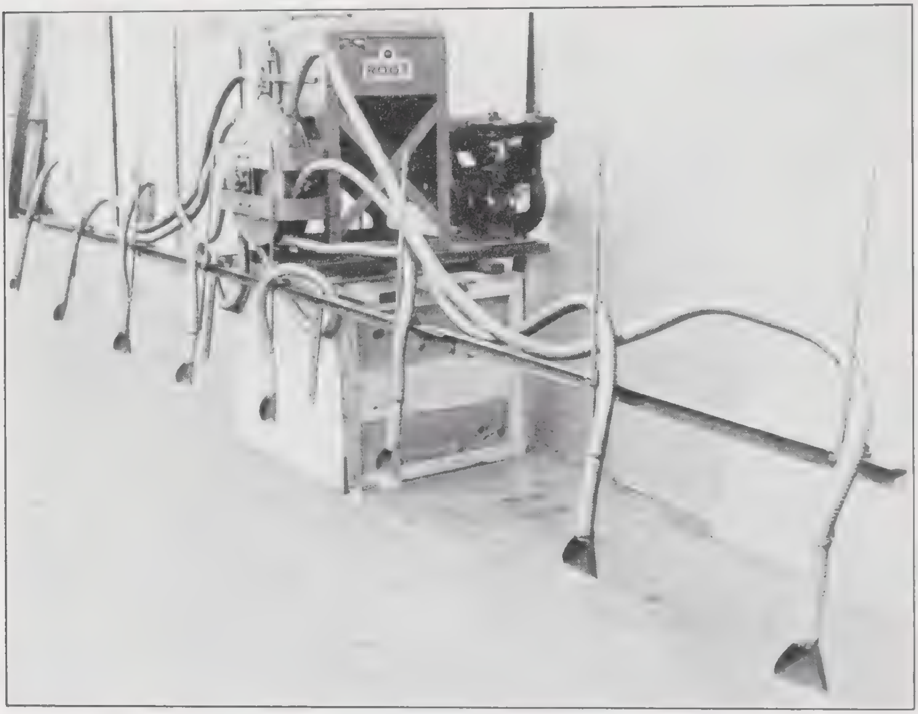

Fig. 28. Boom duster with peripheral delivery manifold. (Courtesy of Brown-Manly Plow Co.)

In the other type of power duster the material is delivered through a single large orifice or circular muzzle. Field crops are treated in strips over which the dust is drifted (drift dusting), or the dust may be aimed at orchard crops. The reinforcing of the air blast to enable large trees to be dusted has led to the development of fan and turbine blowers of tremendous force. For orchard dusting, a manifold of eight nozzles on flexible Y attachments may be arranged like a Catherine wheel on the rear of the duster (e.g. *Naco*), or a pair of large fishtail nozzles may

be directed to either side, so that two rows of trees may be dusted as the machine is towed between the rows. Recently the high-velocity blowers have been replaced by equipment which delivers large volumes of air at low velocity (e.g. *Masterfan*), and which have given more uniform deposits of the dust.[17] The coating of the dust particles with oil or water as they leave the muzzle is even more desirable in the drift-dusting technique, and for this purpose the turbine sprayer-duster was designed. An aqueous emulsion of oil is sprayed onto the dust as it leaves the muzzle, at the rate of 1 gal of liquid to every pound of dust.[13] These blower-dusters have proved to be much more valuable for the application of sprays than of dusts, and in fact furnish the origin of the spray blowers.

No matter how good the agitation and feed in the dust hopper, whether performed by wire drums, worms, or rotary brushes, the delivery rate is very uneven, the deviations having been determined to range from 50 to 300%. Delivery depends not only on the level of the dust in the hopper, but also upon the extent to which it has become packed. However, a superior dust feed has been developed consisting of a vertical auger which elevates the dust to an overflow delivery;[1] the deviations in delivery amount to only 2%, which represents a remarkably even emission.[59]

The substitution of dusting for spraying is especially attractive in hilly or muddy orchards, since it means replacing a heavy tank containing 1500 lb of spray with a light hopper carrying 200 lb of dust. Dusting is also favoured in areas where the water supply is inadequate or inconvenient. The use of dusts eliminates the residue problem associated with late-season spray applications. The process of dusting orchard trees by blowers has been found to be 2–3 times as rapid as high-pressure spraying. However, the greater cost of dust materials raises the cost per tree to a comparable figure.[25] Since dust cannot be aimed to impinge on foliage to any extent, it must largely settle or be trapped by the cuticular hairs or exudations of the plant. Therefore orchard dusting is effective only under conditions of very little wind.[29] For codling-moth control with lead arsenate, it has been concluded that twice as many dust applications as sprays are required for comparable results.[29] In Indiana, a programme based on dusts allowed 15% contaminated apples (stings) against

8% with a spray programme;[23] in Colorado, dusts allowed 17% wormy apples, sprays 2%.[52] In New York, dusts reduced the infestation to 6 larvae per 100 apples, as against 3 when sprays were used.[19] In Connecticut, sprays gave better control of all apple insects than dusts;[120] in Indiana, plum curculio was reduced to 4.5% injury with sprays as against 11% with dusts.[23] Yet in Michigan the same degree of protection was given by lead arsenate dusts as by sprays.[25] It has been observed that there is little difference between the two methods when the infestation is light.[90] It is concluded that dusting of orchards is normally warranted only in the case of a light infestation, or as an emergency measure if the spraying equipment cannot cover the area in 3 days of operation.[18]

Bait spreaders

The typical bait spreader consists of a large horizontal rotating disc onto which the moistened bran-sawdust bait is dispensed from a hopper above it. This is mounted on a two-wheel trailer (generally the rear end of an automobile) so modified that the wheels drive the disc by traction. The bait is spread in swaths ranging from 7 to 10 yd in width.

In an improved model, the USDA Bait Broadcaster, the disc is driven by a 5-hp gasoline engine, so that the spreader may be mounted in the back of a truck. Here the spreader disc is 18 in. in diameter and is furnished with three spreader blades (Fig. 29). The swath widths are found to reach approximately 15 yd.[104a]

For the coverage of large areas at faster speeds, a machine has been developed which blows the bait out by means of a fan. This is the USDA Blower Spreader, which resembles a power duster in principle. It is driven by a 5-hp engine and may be mounted in a truck.[104a] The turbine sprayer-duster has also been used to disperse oil-base bran bait, and a special broadcast nozzle has been attached for emission behind the direction of travel; however, the bait particles have too much momentum to be deflected to the sides of a nozzle as the air is, and so swath widths do not exceed 12 yd. If the fishtail nozzle of the turbine sprayer is employed to emit at an angle of 45° into the air into a light

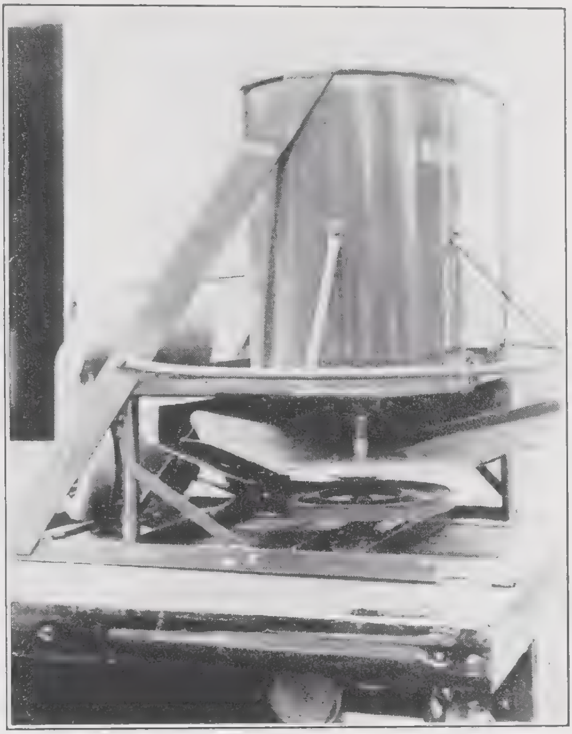

FIG. 29. USDA Bait Broadcaster. (Courtesy of U. S. Bureau of Entomology and Plant Quarantine)

crosswind, a swath width of 25 yd may be obtained. If the round nozzle is fitted with a 10-in. extension and used in a similar fashion, widths of 35 yd can be attained in light (< 5 mi/hr) winds, and 50 yd in moderate (6–10 mi/hr) crosswinds.[116]

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CHAPTER VI

The Application of Insecticides from Aircraft

History of aircraft dusting

The first application of insecticide dust from the air was made in 1921 and 1922 in Ohio by Neillie and Houser with lead arsenate to control the catalpa sphinx* (*Ceratomia catalpae*).[13, 64] In the following year, dusting operations were commenced against the boll weevil and the cotton leafworm in the southern United States, and against locusts in the Philippines. By 1925 aerial dusting against forest insects was under way in Germany,[57] the United States, and Canada, against locusts in the U.S.S.R., and against malaria mosquitoes in the southeastern states. In the pioneer work of 1921 the dust was held in a bin on the side of the aircraft, and it was cranked out through a hole in the bottom. In 1923 Morse installed a hopper in the front cockpit (the Dayton hopper), equipped with an agitator; the dust was emitted into a Venturi tube suspended beneath the fuselage. As a consequence of testing by Coad in 1924, the Huff-Deland-5 aircraft was fitted up for cotton dusting with the unit devised by Morse. Nevertheless, air-suction hoppers, where air was drawn in through a tube

* Although a sack of arsenical dust was scattered over an alfalfa field near Reno, Nevada, in 1918.[59]

extending down through the hopper, which in turn drew in the dust at the bottom and carried it out an emission pipe, were also used in the United States and in Europe in the early years. The Venturi tube is now generally replaced by the pan type of Venturi spreader with a constricted throat. The suitability of the autogyro for insecticide application was first tested in 1937 in Massachusetts,[33] and of the helicopter in 1945 in the United States and Britain.

Aerial dusting in the U.S.S.R. was developed on a large scale by the governmental bureau Aviakhim and its successors, operations being mainly conducted against locusts and malaria mosquitoes.[52] In the United States this activity was largely taken over by private enterprise, so that by 1939 there were between 100 and 200 planes engaged in crop dusting, mainly for the large grower. By 1949, no less than 1883 planes were registered for aerial dusting, 1327 for spraying of insecticides, and 17 for the spreading of grasshopper bait. The industry had received a tremendous stimulus not only from new powerful insecticides, but also from the abundance of war-surplus planes and discharged pilots, and the high market value of crops. Examples of the principal aerial-dusting operations reported in the literature[41] are summarized below.

Forest insects. Aerial dusting with calcium arsenate was commenced against the nun moth (*Lymantria monacha*) in Prussia in 1925 and continued in 1928; DNOC dusts were applied against this insect in East Prussia in 1935. Aerial dusting with calcium arsenate was also practised in Prussia against *Panolis flammea* and continued in 1932 with rotenone. In 1930 this insect was treated with calcium arsenite in the Kharkov district of the Ukraine, and in 1937 with pyrethrum dusts in Franconia. Aerial dusting with calcium arsenate to control the gypsy moth (*Porthetria dispar*) was commenced in Massachusetts in 1926. By 1937 an autogyro was being used, and the dusts were moistened by fish oil added on emission; 1200 acres in Connecticut were treated by this means in 1942. The pine looper (*Bupalus piniarius*) was treated in Germany with calcium arsenate in 1926 and 1929. Control operations were undertaken in Poland in 1929, in Ukraine and central Russia in 1930–31, and in the Urals in 1939, using calcium arsenite. An infested area of 150,000 acres

in Brandenburg was treated with *Forestit* (veratrin dust) in 1931-32.[68] The organic insecticide DNOC was used against this species in Germany in 1936. Infestations of the hemlock looper (*Ellopia fiscellaria*) were controlled with calcium arsenate in Wisconsin in 1926,[30] in Ontario in 1928, in Quebec in 1929, in British Columbia in 1930,[58] and in Washington in 1931. Calcium arsenate dust was used to treat infestations of the oak leaf roller (*Tortrix viridana*) in Westphalia in 1926, and the spruce budworm (*Choristoneura fumiferana*) in Nova Scotia and Ontario from 1927 to 1929.[58] The cedar silkworm (*Dendrolimus sibiricus*) was controlled in the Lake Baikal region in 1929 with calcium arsenite, and in 1940 with sodium fluosilicate. The pine silkworm (*D. pini*) was treated in 1939 with pyrethrum dust in European Russia.

In South Africa, aerial dusting was inaugurated in 1925 against the eucalyptus weevil (*Gonipterus scutellatus*). In 1936 the browntail moth (*Euproctis terminalis*) was treated with calcium arsenate, and in 1938 aerial dusting with cryolite was commenced against the wattle bagworm (*Acanthopsyche junodi*). In Australia, infestations of the pine case-moth (*Cryptothelia tenuis*) in Victoria were dusted with calcium arsenate in 1931.[41]

Locusts and crickets. The migratory locust (*Locusta migratoria*) was first treated with calcium arsenate in the Philippines in 1923 and again in 1928. Russian experiments started in 1924 with sodium arsenite in Turkestan. Between 1925 and 1929 applications were made in the Kuban, North Caucasus, and Astrakhan regions with sodium and calcium arsenite. Applications were made with sodium arsenite in Dagestan and the Uzbek republic in 1932, and in Kazakhstan in 1935. The Moroccan locust (*Dociostaurus maroccanus*) was controlled by aerial dusting in Azerbaijan, Caucasus, in 1931, and in the Uzbek and Tadzhik republics of Central Asia in 1934. An outbreak of *Schistocerca paranenis* in Argentina in 1947 was treated with DNOC dust from airplanes and helicopters. Swarms of the red locust (*Nomadacris septemfasciata*) were treated from the air in Rhodesia with sodium arsenite dusts from 1934 to 1939, being more vulnerable when at rest than in flight. The desert locust (*Schistocerca gregaria*) was dusted with DNOC in Kenya

in 1944, and in northern Iran by the British and Russians in cooperation.[39]

***Anopheles* mosquitoes.** Aerial dusting with Paris green was developed in 1923, and by 1926 it was in full swing in Louisiana[90] and Virginia. In 1928 it was being practised in Italy. From 1929 to 1939 the U.S.S.R. carried out malaria-control operations with this chemical in the areas around Moscow, Smolensk, Kiev, and Kuibyshev; in the eastern Ukraine, North Caucasus, Armenia, and Azerbaijan in Transcaucasus; and in Kazakhstan east to Lake Balkhash. In 1932 it was practised in the French colonies of Madagascar and Indo-China, and in 1937 in northern India. The Tennessee Valley Authority started operations with Paris green in 1937,[91] and in 1944 six southern states were still using it. The German Luftwaffe used it for malaria control in Greece and the Ukraine in 1941, but by 1943 had replaced it with thiodiphenylamine (phenothiazine). The poor dusting qualities of DDT led to the development of aircraft spraying for malaria-mosquito control during World War II.

Cotton and sugar-cane insects. In 1923 the practice of cotton dusting with calcium arsenate against the boll weevil (*Anthonomus grandis*) and the cotton leafworm (*Alabama argillacea*) was incepted and spread to all the cotton-growing states. In 1926 nicotine dusts were added to control the cotton aphid (*Aphis gossypii*). In 1928 aerial dusting was introduced into Peru to control these cotton insects and the cotton stainer (*Dysdercus ruficollis*). In 1930 the Russians dusted cotton with calcium arsenite to control the cotton bollworm (*Heliothis armigera*) in Kazakhstan. Between 1930 and 1933 they dusted cotton with sulphur to control the mites *Tetranychus telarius* and *Epitetranychus altheae* in Kazakhstan and Armenia. Control of the sugar-cane borer (*Diatraea saccharalis*) in Louisiana was commenced in 1925 with sodium fluosilicate, which was in later years replaced by cryolite. The dense cane thickets render airplane dusting the only possible treatment.

Orchard insects. The first experimental application was made in 1922 in England in an attempt to control the cherry tortrix. In 1925 private enterprise in Indiana demonstrated the feasibility of dusting apple orchards. In 1926 peach orchards in Georgia were dusted with lead arsenate to control the plum cur-

culio (*Conotrachelus nenuphar*). In 1929 citrus orchards in California were dusted with sulphur to control *Scirtothrips citri*. In 1930 orchards in Russia were dusted with calcium arsenate to control *Hyponomeuta padella*, and in 1932 control of the codling moth with this chemical was commenced in the Uzbek republic of Central Asia. At the end of World War II, the dusting of apple, pear, cherry, and peach orchards was commonplace in the United States, and increasing attention was being paid to helicopters [19] to overcome the disadvantages of fixed-wing planes in reaching the undersurfaces of foliage deep in the crowns.

Field-crop insects. In 1926 aerial dusting of crops with calcium arsenate was commenced against *Heliothis armigera* on tomatoes in Mexico and against the alfalfa weevil (*Hypera postica*) in Utah. The dusting of blueberry bogs with calcium arsenate for control of apple maggot (*Rhagoletis pomonella*) was developed in Maine and New Jersey between 1927 and 1931. Aerial dusts of pyrethrum were used in 1935 to control the leaf hopper *Ophiola striatula* in the New Jersey cranberry bogs. The annual coverage of crop dusting with calcium arsenate in California had reached 140,000 acres by 1930. In that year the Russians first tried the aerial application of calcium arsenate on the beet webworm (*Loxostege sticticalis*) in the Ukraine, in 1932 used it on insects destroying mustard fields, and in 1939 dusted sodium fluosilicate against the beet weevil (*Cleonus punctiventris*). In 1942 an aerial control programme was carried out with calcium arsenite against *Eurygaster integriceps* in the wheat crop of the Uzbek and Kirghiz republics. Between 1945 and 1950 nearly every type of field crop in the United States, particularly corn, alfalfa, tobacco, potatoes, peas, and onions, was being commercially treated from the air with insecticidal dusts, which most commonly contained DDT.

History of aircraft spraying

The first recorded experiments in aircraft spraying were made by Russian workers in 1922 near Moscow, using vermorel nozzles and pressure feed.[67] However, since the favoured insecticides of the next two decades were arsenicals insoluble in liquids, spraying was abandoned in favour of dusting. In 1932 kerosene was sprayed from rotary brushes for mosquito larvicidal work, and

in 1933 miscible oils were similarly applied to orchards, vineyards, and truck gardens in California.[12] In 1936 tests were made with oil solutions of pyrethrum against the beet leaf hopper (*Eutettix tenellus*),[16] and in 1938 with oil solutions of rotenone and nicotine against the pea aphid (*Macrosiphum pisi*) in New Jersey. From 1936 to 1939 the spraying from airplane or autogyro of suspensions of lead or calcium arsenate was developed in Massachusetts[33,72] for gipsy-moth control, and by 1942 cryolite suspensions were being sprayed in Connecticut, New York, and Pennsylvania. In 1941 and 1942 the Russians were spraying calcium arsenate suspensions for control of cotton bollworm in North Caucasus and Transcaucasia.

The arrival of DDT, soluble in aromatic oils, and so highly insecticidal that the solution could be sprayed very thinly and still be effective, brought aircraft spraying into its own. After tests in Florida in late 1943,[57] the United States Air Force and the Royal Air Force in 1944 sprayed oil solutions of DDT for control of malaria mosquitoes from wing tanks of fast fighter and reconnaissance aircraft in Italy and the islands of the southwest Pacific area; while extensive trials with larger aircraft in Florida, West Africa, British Guiana, and Panama set the stage for more extensive malaria-control programmes in the southwest Pacific and Burma-Assam theatres in 1945. By the end of the war the main aircraft used for spraying were light planes such as the Piper Cub (L-4) and Stearman (PT-17) fitted with nozzles, and heavier ships such as the Mitchell (B-25) and the Dakota (C-47) fitted with vertical emission pipes.

Concurrently civilian authorities developed aircraft spraying of DDT against forest insects. In 1944 it was applied against the pine looper in Sweden and against the gipsy moth in Pennsylvania.[11] In 1945, 100 sq mi of spruce and fir forest were treated in northwestern Ontario with DDT at 1 lb/acre for control of the spruce budworm, using a Canso (Catalina) PBY seaplane;[56] 45 sq mi were treated in the following year.[18] In the same year DDT was sprayed over 12,000 acres of forest in Oregon for control of the hemlock looper, using Waco biplanes. In 1947 a single operation to control the fir tussock moth (*Hemerocampa pseudotsugae*) in Idaho involved 413,000 acres

being sprayed with a solution of DDT at 1 lb/acre, all types of planes ranging up to the C-47 being employed.[25]

Spraying methods with large aircraft have also been developed for locust and grasshopper control. The spraying of DNOC in oil solution for control of the desert locust was carried out in Kenya in 1945 with Baltimore aircraft.[39] Although settled swarms were the best targets, flying swarms could be attacked by laying down a falling curtain of spray across their line of flight.[36] The technique was continued in 1947, using BHC and DNOC solutions against the red locust in Tanganyika;[38] 11,000 acres in the Rukwa valley were cleared of locusts on the ground by spraying 3300 acres from Anson XIX aircraft. Aircraft sprays have been used in Canada against grasshoppers, with small planes and large, since 1945.[12] A total of 215,000 acres were sprayed from the air in 1948 in Illinois alone.[59] A large control operation, using toxaphene and chlordane, was completed in Wyoming in 1948, using a Douglas C-47 equipped with boom and nozzles. In 1950, a fleet of small aircraft (N-3-N, etc.) obtained 98% control of *Melanoplus leukinus* over 40,000 acres in the Sulphur Springs valley of Arizona with sprays of aldrin in oil applied at 2 oz/gal/acre.

Malaria control by aircraft spraying has been carried out in many parts of the world, notably the southern United States, Venezuela, Greece, and Singapore. Cholera epidemics in Manila in 1946 and in Cairo in 1947 were prevented by spraying DDT to control houseflies. Many towns in the central United States have been similarly sprayed as a measure against poliomyelitis. The aerial spraying of summer resorts and the outskirts of cities to remove the nuisance of mosquitoes is a frequent practice. The costs involved compare favourably with those of ground application.[95] Since 1947, attempts have been made to render summer conditions endurable at stations in northern Canada[87] and Alaska[88] by spraying DDT over large areas from C-47 planes to control *Aedes* mosquitoes. Northern rivers have also been sprayed from the air to eliminate *Simulium* blackflies in their breeding grounds.[5] In 1948, tsetse-flies (*Glossina* spp) were almost eliminated over 100 sq mi in south-central Africa by an aerial spray of DDT.[24] Aerosols of DDT in oil have also been applied with great success from Anson aircraft against tsetse in

Zululand,[15] and from helicopters against blackflies in New York State and against adult *Simulium damnosum* in the Belgian Congo.

For aircraft spraying against crops, suspensions of wettable powders in water are generally employed, owing to the danger of phytotoxicity from oil solutions or emulsions. Corn, potatoes, and alfalfa are the main crops treated, the acreage concerned being especially large in the United States. In 1949 a concerted attack was made to eliminate the potato beetle (*Leptinotarsa decemlineata*) from the Cherbourg peninsula of France by aerial dusting and spraying of DDT from fixed-wing planes and helicopters. In the United States the ratio of aircraft sprayers to dusters had risen from 1:15 in 1946 to 1:1 in 1949.[59]

History of aircraft baiting

The broadcasting of sodium arsenite in a moist carrier as bait for locusts was commenced in Russia in 1930, and experiments in Uzbekistan determined the conditions deciding width of swath. After an individual attempt in North Dakota in 1930, application of arsenic-bran-molasses bait was made in 1931 over 10,000 acres in Iowa to control grasshoppers. The practice grew with commercial operators in the United States, so that by 1939 in a single year 260,000 acres in Montana was treated from the air against *Melanoplus mexicanus*, and air operations were commencing in California. The aircraft dusting operations which had been conducted in Nevada against the Mormon cricket were replaced by baiting from aircraft in 1941. Between 1934 and 1941 a total of 122 million acres had already been treated in the western United States by bait spread from small aircraft. In 1947 a Douglas C-47 was equipped for large-scale dispersal of bait in Alberta and Saskatchewan, and in 1949 a large area was treated with a plane of this type in Wyoming.

Advantages of aircraft application

Speed. With crop dusting and spraying, aerial application allows from 500 to 2000 acres to be treated in a day, although applications may be limited to 3 hr of that day. In mosquito larviciding with large planes, a square mile may be treated in a half-hour. In forest insect control, aircraft have been able to

spray half a million acres in 6 weeks. The advantage of speed is that a control operation may be completed within the time limits set by the habits of the insect pest. This in turn means that an even larger **area** may be included within the bounds of timeliness, and thus infestations of considerable extent can be controlled quite expeditiously.

Accessibility. There are some types of vegetation which can be reached only from the air; sugar cane is an outstanding example. The crown cover of forests can be reached from the ground only with great difficulty, from the air with ease. Swamps and marshes are easily accessible from the air only. Jungle and northern forest alike may be thoroughly treated only from the air. The regions where locusts and grasshoppers breed are generally inaccessible by road. Even in regions served by roads, the convenience of loading the aircraft with insecticide at a properly equipped station and flying straight to the area puts the old-fashioned ground approach at a disadvantage. The aerial applicator is independent of the hazards of muddy footing in approach or field, which may immobilize ground equipment. Finally, the ability of air application to treat the crop without mechanically disturbing it in any way puts it at an advantage even in heavily settled regions where high-priced crops are grown.

Economy. Aerial spraying effects a saving in machinery. The availability of custom spraying services in the district releases the farmer from making a heavy investment in specialized farm equipment, which is used only for a short period of the year. Aircraft application also effects a saving in manpower, which at certain times becomes crucial. These economies enable commercial aviation to compete successfully in the field of insect control.

Disadvantages of aircraft application

One of the more serious shortcomings of fixed-wing aircraft as crop dusters is that the underleaf coverage may be less than with ground application. For this reason a lower level of control was obtained from the air than from the ground with cryolite against potato flea-beetles, and with rotenone against the Mexican bean beetle. But when DDT was used against *Empoasca*

and *Lygus* on beets, and against hornworm and flea-beetles on tobacco, air applications were completely successful. With DDT or rotenone against the pea aphid and pea bruchid, the control was just as good with fixed-wing aircraft as with ground applicators.[3] Helicopters will give adequate underleaf coverage against those species for which this factor is critical.

The use of aircraft has hitherto been jeopardized by the possibility of delay due to weather or mechanical trouble. Another disadvantage is the comparative lack of contact of the applicator with the ground it treats, and the consequent uncertainty as to results. However, development in technique and skill should eliminate the latter disadvantage, and should be able to push operation to the limits of weather which would immobilize ground equipment also.

Another material disadvantage of aircraft application is the high element of risk, reflected in extremely high insurance rates. Between 1943 and 1948, 10% of the agricultural aircraft in the industry were destroyed by accidents. It is probable that these drawbacks may be largely overcome by using suitable types of aircraft. It has been suggested that the most suitable type is a low-wing monoplane, of all-metal construction with bolted wing-sections, powered by not less than 200 hp to carry a 1250-lb payload at 60–70 mi hr.[40a] The Flying Farmers of America have developed an agricultural monoplane with a payload of 2000 lb contained in tanks at the wing bases, a cruising speed of 60 mi hr, and a landing speed of 40 mi hr. In Canada, a spray-boom installation has been commercially developed for the De Havilland Beaver, an aircraft with considerable reserve power.

Advantages of spraying over dusting from aircraft

Less drift. Whereas dusts should not be applied at wind speeds in excess of 3 mi hr, spraying may be satisfactorily performed on some crops at wind speeds up to 10 mi hr[34] and on large areas up to 20 mi hr. Aircraft spraying may be carried farther into the morning and started earlier in the evening than dusting, and on overcast days it may be continued all day.[27] Spraying may be carried out effectively from greater heights than dusting, because the larger, spherical droplets of spray fall faster through air than the small, irregularly shaped dusts; they

pick up momentum quickly and can be aimed to travel on a known path, whereas dusts cannot safely be entrusted to the vagaries of any depth of air. With sprays, usually over 60% of the material emitted is deposited on the target, the percentage recovery ranging from 30 to 95%;[33] with dusts the range is from 20 to 60%.[60] The deposit is increased the coarser the spray, the greater the specific gravity of the liquid, and the cooler the air temperature.[19]

Better deposit. Whereas dusts do not adhere well to foliage unless dew is present, and are easily washed off by rain, sprays will readily impinge and spread upon dry foliage. Spraying planes equipped with booms and nozzles produce a much more even deposit than aircraft dusters equipped with the Venturi spreader. Consequently it may be found that a spray achieves equal results with two-thirds as much insecticide as is employed in the dust, and that a single spraying may produce the control that demands up to four dust applications.[34]

Greater flexibility. The technique of aircraft spraying allows ready adjustment of dosage rate, droplet size, and formulation at any time.[20] This is not the case with aircraft dusting, where the particle size is fixed, the concentration of insecticide is not readily altered, and the emission rate cannot be greatly reduced without risk of uneven deposits.

Installations for aircraft spraying

Booms and nozzles. In these dispersal systems a horizontal boom of ¾- or 1-in. steel tubing is suspended beneath the wings. The boom is divided into two parts by the pump below the fuselage. It is fitted with nozzles of the flat-fan or hollow-cone type, spaced roughly every 4 in.; for example, a 193-in. half-section of boom on the L-4 Cub has been fitted with 45 nozzles, and a 150-in. half-boom on the N2S Stearman with 42 nozzles.[14] In some cases the nozzles are arranged in clusters 8–12 in. apart.[1] The spacing of the nozzles should be closer at the boom ends where the pressure is lower; this applies especially to small-bore tubing, since pressure loss with length of pipe varies inversely as the fourth power * of the diameter.[31] Normally the nozzles point

* Although experiment has shown pressure loss to vary inversely as the diameter raised to the power of 2.8.

backwards, but they may be pointed downwards or even slightly forwards to decrease the droplet size.[19] In a biplane such as the Stearman the boom is suspended 9 in. below the lower wing and midway between the front and rear spars; if it were located farther forward it would endanger off-balance landings;[34] it is considered by some that the optimum location is at the trailing edge of the wing, where the vertical velocity component of the air flowing off the wing is at a maximum.[32] In high-wing monoplanes such as the L-4 Cub the two halves of the boom may be carried obliquely from the fuselage to the wing tips. Or they may be suspended horizontally, in which case they are shorter than the wings. In the Lysander aircraft the boom is carried below the bomb step above the landing gear. The nozzles on some booms may be spaced quite widely, the extreme case being the N3N installation, where there are only double nozzles at each

TABLE 1. Approximate Loads and Speeds of Aircraft Employed in Insect Control[25,76,81]

Type of Aircraft	Load, lb	Speed, mi/hr
Taylorcraft (L-2), Aeronca (L-3), Piper Cub (L-4)	250	70
Stinson (L-5), Fairchild (PT-19)	400	90
Stearman (PT-17 or N2S-3), Navy N-3-N, Waco-9	500	90
Vultee (BT-13), Norseman (C-64)	1000	120
Stearman 4-D, Stinson SM7A, Travelair	1500	90
Anson XIX	1500	150
Ford Trimotor	3000	90
Canso Catalina (PBY)	6000	135
Douglas Dakota (C-47)	7500	150

wing tip, interpolated by a double nozzle below the tail assembly.[14] In the metal wings of the large C-47 aircraft, booms have been placed inside the wing, with nozzles protruding at the trailing edge; a suspended boom has also been developed for this aircraft.[44a] By carrying the system of nozzles out to the end of the wings, advantage may be taken of the wing-tip vortex to obtain wider swaths. The nozzles are provided with spring-loaded check valves to stop emission when the spray-control valve is closed.[32] The nozzle seatings should be exposed so that the orifices may be unplugged by wire cleaners. A system has

been developed whereby spray cut-off releases a jet into a Venturi tube which sucks the liquid back; the ball valves prevent the booms being emptied so that emission is immediate when the main valve is opened again.[1] The spray tanks are mounted in the fuselage or cockpit as close to the centre of gravity as possible. In certain cases, such as the Silvaire sprayer and the Canso PBY, they are located in the wings. Their size is governed by the load capacity of the plane, approximate figures for various aircraft being given in Table 1. Normally they drain into a line leading to a pump, which impels the liquid under pressure into the booms and out through the nozzles. A quick-acting spray-control valve is inserted between pump and booms. Between pump and spray-control valve there is a hydraulic relief valve, whose adjustment for pressure may be modified to the desired level for the particular application. The superfluous discharge from this valve is conducted back to the bottom of the tank to provide agitation. In small planes flying under hazardous conditions the tanks may be provided with an emergency dump valve.[14]

The pumps are either rotary-vane or centrifugal types. For crop spraying, single-stage centrifugal pumps are used, since they alone can handle unharmed the abrasive suspension sprays generally applied to crops. Normally they generate a pressure of 30–40 psi,[31] with the extreme range 20–100 psi.[1] In mosquito control, and in certain agricultural work where emulsions and even oil solutions can be employed, gear pumps or rotary-vane pumps are used, with pressures ranging up to 120 psi. The output capacities required vary according to the requirements of the plane and the application, but for light planes they are between 15 and 30 gpm,* where the job calls for 5–10 gpm actual delivery (see Table 2). The pumps are driven by windmill propellers mounted outside the fuselage. They are 18–20 in. in diameter, with 4 wooden blades set at a pitch of 33–35°. At a flying speed of 90 mi/hr they rotate at 2000–2500 rpm. When not in use they are externally braked.[11] The swath width obtained with small aircraft such as the L-5 Stinson, Lysander, Stearman

* In this chapter, volumes are given in U. S. gallons; 1 gal (U. S.) = 0.83 gal (Imperial).

PT-17 and N2S-3, and Navy N-3-N is 35 yd[10a] (Fig. 1). With the L-4 Cub the effective swath width for the spraying of corn was limited to 19 yd.[11] The C-47 equipped with nozzles extending to the wing tip achieved a swath width of 260 yd with a spray of 140-μ mass median diameter for control of mosquitoes in

Fig. 1. Spraying with boom-and-nozzle assembly on a Cub-type aircraft. A. Front view. B. Side view. (Courtesy of AGSCO, Inc.)

Alaska.[88] The strip interval selected for spraying full-foliaged crops is generally between 1 and 1.5 times the width of the boom installation.

Breaker bar. This is a simple boom of 1-in. tubing carrying a series of drilled orifices in place of inserted nozzles, which can be readily mounted or dismounted on a small aircraft. It proved of great value in the southwest Pacific war theatre for equip-

ping Army L and PT planes and Navy TBM and TBF aircraft. The orifices are from 1.5 to 6 in. apart, 0.03–0.07 in. in diameter, and are faced backwards to discharge against a breaker bar attached parallel to the boom and 0.5 in. away from it. The breaker bar is 1 in. wide by 0.25 in. thick, with a flat or 5° convex face. The improved breaker bar is bent forwards above to form an air scoop and angled backwards below to form a drag-bar off whose trailing edge the spray film is atomized; the air scoop forces the droplets downwards into the propeller wash.[102] The bar may be replaced by screen frames, 16–40 mesh, when fine atomization is desired.[45] On the TBF and TBM naval

TABLE 2. Emission Rates and Droplet Sizes (in Microns) of Sprays from Aircraft [77,100]

Apparatus	Aircraft	Emission, gpm	Pressure, psi	Droplet Diameters: Frequency Medians, By Number	Droplet Diameters: Frequency Medians, By Mass	Droplet Diameters: Largest Droplet
Boom and nozzles	Stinson L-5	4	50	100	175	300
Breaker bar	Stinson L-5	10	120	75	150	250
Husman-Longcoy	Stearman PT-17	7	100	100	150	350
Spinner disc	Stearman PT-17	9	Gravity	75	150	350
Exhaust Venturi	Stearman PT-17	1	70	40	60	100
Straight pipe	Douglas C-47	100	Gravity	180	330	1120

planes, the breaker bar is suspended 12 in. beneath the wings; on the L-4 Cub and L-5 Stinson it is mounted horizontally 4 ft beneath the wings, and on the PT-17 Stearman 9 in. below the lower wing.[51] The spray is emitted at pressures between 25 and 120 psi[77] and at rates from 10 to 15 gpm. The swath widths obtained with this equipment installed on planes flying at 35-ft altitude in still air were 27 yd with the L-4, 40 yd with the L-5 and PT-17, and 50 yd with the TBM flying with flaps partly down.[45]

Husman-Longcoy unit. This portable unit, developed for easy installation into Army liaison and trainer aircraft, consists of a row of nozzles mounted at the trailing edge of a subfuselage

Venturi air scoop similar to that used in aircraft dusting equipment. Since a high emission rate (0.6 gpm) is required, fern-type nozzles with large orifices are used. For the L-4 and L-5 aircraft, 6 nozzles give a total emission of 3.5 gpm at pressures of 50 psi; for the PT-17 Stearman, 12 nozzles give 7 gpm at 100 psi. The Husman-Longcoy unit may be expected to give a swath width of 25 yd.[51]

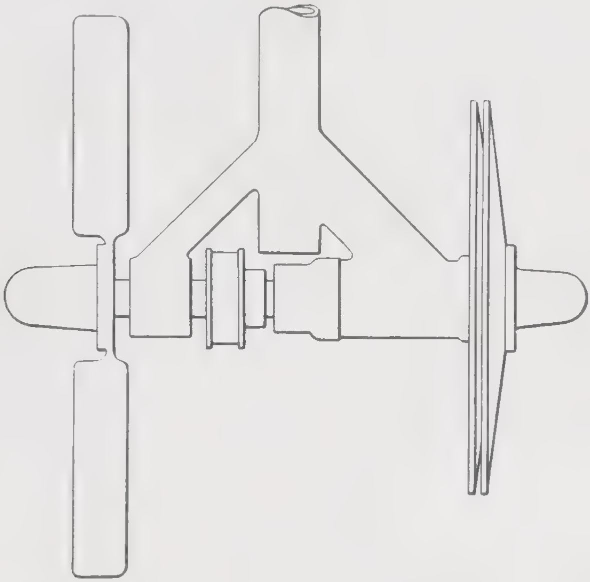

FIG. 2. Diagram of spinner disc apparatus. (From *U. S. Dept. Agr. Pub.* **EC-2**)

Spinner disc. This unit was devised to deliver heavy suspensions (e.g. lead arsenate, cryolite, DDT) which would prove abrasive to a pump. It is fed by gravity, the only pressure being the head in the tank. It consists of a sandwich of two concave discs spaced $^1\!/_8$ in. apart, into which the spray suspension is fed by a line entering a cavity in the centre of the discs (Fig. 2). The spray is thrown off when the 14-in. discs rotate at about 2500 rpm. Power to rotate the discs is provided by a windmill propeller mounted on the same shaft. Two spinner-disc units may be mounted on a White Standard biplane, to project 6 ft on either side of the fuselage and clear of the slipstream, with the propeller ends facing forward.[11] The emission rate of an installation of 2 spinner discs with a 110-gal tank is 9 gpm, but

as the tank empties this rate may be halved. When a mixture of xylene and fuel oil (1 to 3) was emitted at 8.8 gpm, the mass median diameter of the spray was 100 μ, with 90% of the mass in droplets less than 200 μ in diameter. This equipment obtains a swath width of approximately 33 yd.[77]

Rotary brushes. These units consist of steel-bristle circular brushes 10–12 in. in diameter driven by a windmill propeller on the same shaft at 2000–3000 rpm.[1] One unit is mounted on each wing. The spray liquid was originally supplied from the fuselage tank on Stearman aircraft by 2 centrifugal pumps, allowing emission from 5 to 100 gpm.[12] Now the liquid is held in two 30-gal wing tanks in the Silvaire aircraft, and flows to the brushes by gravity. These brushes are suspended 3 ft below each wing, and the spray is driven downwards by flap action. By selecting the diameter of brushes used, sprays of 10- to 1500-μ average size may be obtained, with a swath width of 15–20 yards when the aircraft is flown at 5- to 6-ft altitude.[1] Fog below 50-μ size is produced by fine brushes spinning at more than 3000 rpm, and spray above 50-μ size by coarse brushes rotating at less than 3000 rpm.[15a] Another spinning contrivance consists of propellers with 3 hollow blades, with jets set in small Venturi tubes at their tips.[42]

Spray Venturi systems. A gravity-feed system has been developed commercially which consists of 6 Venturi tubes evenly spaced across the lower wing of a biplane. The tube comprises an entrance and exit cone leading to and from a throat, into which the spray liquid is fed by a dispensing valve, not an atomizing nozzle. The suction of the tube is sufficient to maintain a considerable negative pressure for even delivery by the gravity feed employed (e.g. Burnum sprayer).

Suspended tanks. Experiments are in progress with 75-gal tanks which are suspended beneath the fuselage of an N2S Stearman by a bomb shackle. The tanks are standard United States Air Force issue and are fitted with an underwing spray boom, a pump, relief-valve return, and outboard propeller.[27] The spray valve is controlled from the cockpit, and emission may be varied from 5 to 14 gpm. Suspended tanks saw service in mosquito control in World War II in the form of 30-gal M10 tanks and 250-lb SCI's (smoke-curtain installations). These torpedo-shaped ob-

jects were carried on wing racks in Hurricane or Mustang bombers; on release air is scooped into the tank from in front and the spray is emitted behind. Light bombers such as the Beaufort or Boston (A20) can carry two M33 tanks each of 90-gal capacity. Emission rates may be varied from 0.5 to 5 gal/sec.

FIG. 3. Vertical discharge pipe on a C-47 Dakota aircraft. (Courtesy of Defence Research Board of Canada)

Vertical discharge pipe. With this installation, suitable for fast aircraft, the spray is emitted from a pipe carried vertically downward for a distance of 18 inches below the fuselage to clear the slipstream (Fig. 3). The forward velocity of the liquid as it leaves the aircraft (150 mi/hr in the instances used) is sufficient to cause it to shatter immediately it strikes the comparatively still outside air. In the Douglas Dakota used in Canada against mosquitoes and grasshoppers, the end of the pipe is cut at an oblique angle facing rearwards. The average emission rate is 3.7 gps when a 4-in. pipe is used; with a pipe 2.5 in. in diameter the emission rate averages 2.4 gps for the whole tankload. The rate will vary according to the viscosity of the liquid used and the amount of head in the tanks. In the Avro Anson XIX used for anti-locust work in Africa the pipe is bent rearwards at its tip and is fitted with a 2.5-in. iris diaphragm which allows emission rates to be modified as desired.[90] Mushroom valves operat-

ing against spring loading, or gate valves, are used for control of emission. When the straight emission pipe on the C-47 aircraft is replaced by a washboard-type grid of parallel tubes with multiple orifices, a finer spray is achieved (125-μ mmd as against 350-μ), but trials in Panama indicated it shows no superiority for mosquito control. When the straight discharge pipe was compared with an exhaust Venturi tube for control of adult *Anopheles* in Florida woods at the dosage level of 0.3 lb/acre, the two types of sprays were found to be equally effective.[21] In an installation on the Canso PBY aircraft, a series of ¼-in. orifices was drilled in an 8-ft boom located within the slipstream on either side of the fuselage.

These installations are operated by gravity flow, with its inevitable handicap of a decrease in flow rate with decrease in hydrostatic head. Delivery rate bears a logarithmic relationship to thrust, which is directly proportional to the head; the plot of log delivery against log thrust is linear.[47] With one of the two 330-gal tanks installed in the Dakota aircraft, the delivery rate fell from 3.0 gps with a full tank down to 1.8 gps when 50 gal were left in the tank. With one of the two 90-gal tanks in the Anson, the rate fell from an initial 2.6 gps to a final 1.2 gps. In the C-47 installation with multiple-orifice grid, a light pressurization of the tanks with 3 psi from a motor-driven pump was sufficient, when combined with the 2 psi contributed by the suction of the slipstream, to give an even flow rate with a fall-off of less than 8%.[25] Gravity-flow tanks have also been pressurized for boom-spraying work with nitrogen taken from a cylinder through a reducing valve.[73]

The Canso PBY is flown at 66-yd strip intervals,[53] and the C-47 equipped with grid dispenser at 135-yd intervals.[25] The width of the swath attained with these installations is not so much a function of the apparatus as of the turbulence and horizontal movement of the air between aircraft and target. When the role of wind is not only accepted but also utilized, by adjustment of the height of flight to the speed of the crosswind, the effective swath width of the C-47 with straight emission pipe may be increased to 200 yd[59] (see below under Porton method of spraying).

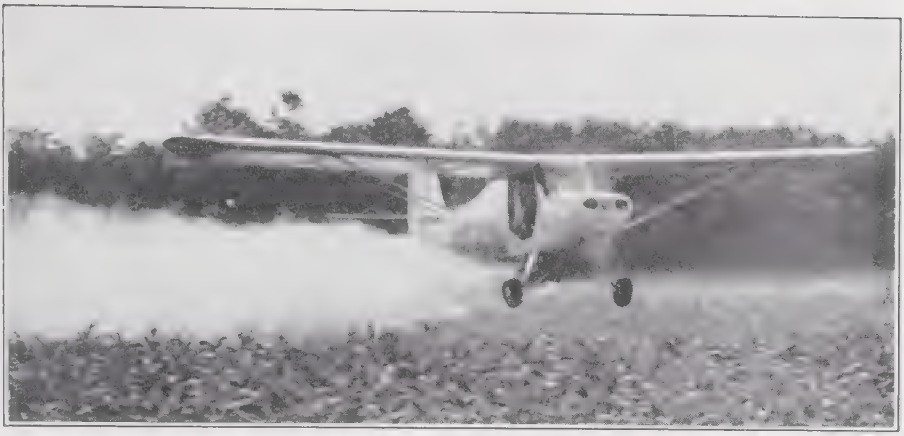

FIG. 4. Dusting of tobacco with Cub-type aircraft; note the Venturi spreader below the fuselage. (Courtesy of Canadian Industries, Ltd.)

Installations for aircraft dusting and baiting

Standard duster. This consists of a hopper inserted in the front cockpit, a wind-driven agitator, a feed-control gate, and a Venturi spreader suspended below the fuselage. The unit is mounted in small aircraft such as Cubs and Stearmans. The hopper is built of aluminum (24ST) or plywood, and the sides slope at not less than 45° to the horizontal down to the throat. There are one or two agitators, preferably of piano wire, which revolve at 50–300 rpm. They may be operated off the outboard propeller at a ratio of 50 to 1, or run directly from electric motors or power take-off. The feed control may be a butterfly valve but is more often a horizontally sliding gate made of aluminum or bakelite (e.g. Micarta). Its closing edge should be cut to a knife edge if it butts, or should slide into flanges below the hopper, to prevent clogging; closure may be made secure by felt seals.[32] The Venturi air-scoop is 30 in. wide, and consists of an apron 8 in. below the fuselage skin and rising to form a throat 3 in. from the skin at the point where the dust leaves the hopper gate; it also may be constricted laterally (Fig. 4). Its effect is to throw the dust clear of the propeller wash into the wing downdraft, so that it is discharged downwards and does not enter the plane.[15] The rate of dust feed through the gate is generally erratic. The rear part of the Venturi scoop is broadened into a fan, with vertical baffles, or divided into two separate outlets, to

spread the dust horizontally.[11] Light planes can carry from 250 to 500 lb of dust, although the Stearman has been reported to carry up to 1000 lb. Emission rates range from 1.6 to 5 lb/sec. The swath width obtainable with the Cub J3 aircraft ranges between 10 and 15 yd[46] (Fig. 5).

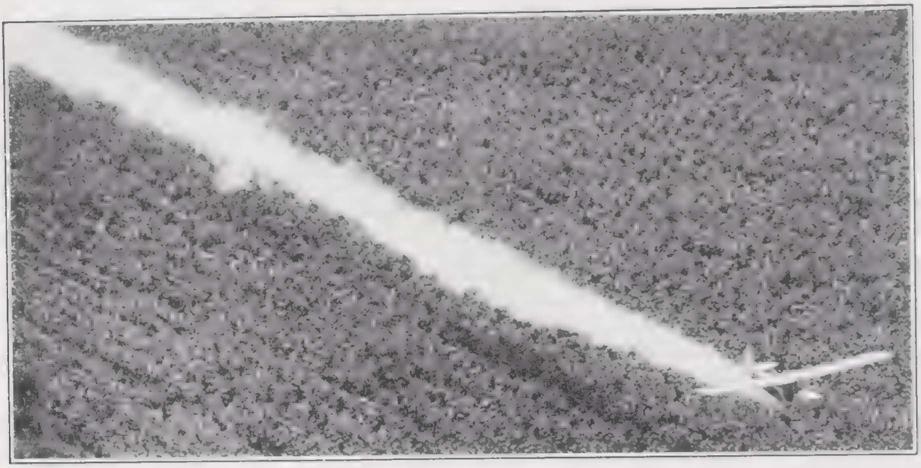

FIG. 5. Crop dusting with Cub-type aircraft; note narrowness of swath. (Courtesy of Canadian Industries, Ltd.)

Breeches-type duster. Here the lower part of the hopper is W-shaped in vertical cross section; it leads to 2 sets of triple shutters and is emitted into 2 Venturi-shaped horizontal emission tubes located on either side of the lower part of the fuselage. In an interesting installation fitted into the Focke-Wulff 58 by the Germans for use against mosquitoes and locusts in the Russian Kuban in 1943, air was forced into the top of the 27-ft^3 hopper by Pitot tubes, the 2 delivery throats had anti-clogging grids, and a rotary agitator was operated from a 25-volt electric motor.[3a]

Suspended tank. Experiments have been made on 75-gal jettisonable gasoline tanks fitted with a new lower section and a windmill-driven agitator. The gate consists of 14 crosswise matching slots, operated from the cockpit. The tank holds 250–400 lb of dust, emitting it at the rate of 2–3.5 lb/sec.[29]

Bait dispensers. The standard duster may be used for dispersing grasshopper baits of sawdust, bran, or oatmeal, although for wet bait the hopper walls should be steeper, with an angle of

at least 55° to the horizontal. The subfuselage air-scoop is omitted, since it does not broaden the swath of the heavier bait. It is desirable to deliver the bait by some metering device, such as a vertical worm in the throat, or a belt conveyor below the gate operated from an outboard propeller.[11] A horizontal worm rotating at the bottom of a long trough-like hopper is being used in the C-47 aircraft.

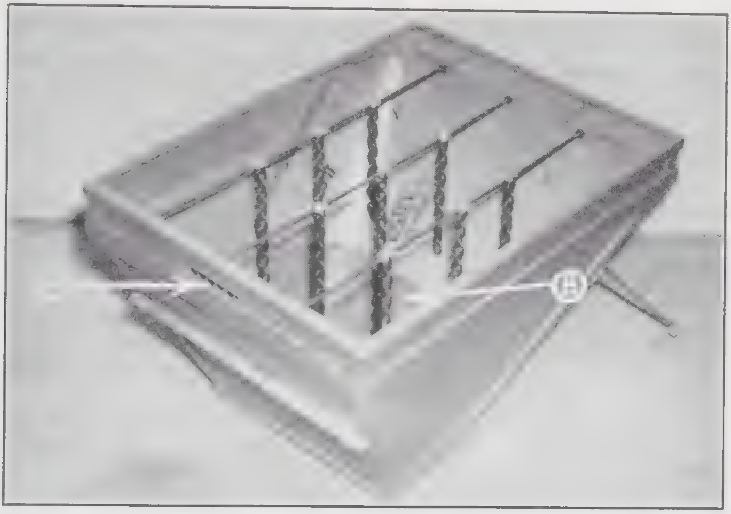

FIG. 6. Suction-feed hopper for bran-sawdust baits for grasshoppers, showing (A) air-inlet holes at top of rearward side, and (B) perforated lower section of false wall. (Courtesy of Defence Research Board of Canada)

Bait hoppers have been designed without mechanical agitators; delivery is aided by utilizing the suction of the slipstream. In one model built for the C-64 Norseman this air is brought in through a perforated inner wall of a double-walled hopper, and pulls the bait out with it when the gate is opened[69] (Fig. 6). Satisfactory emission at rates ranging from 7 to 20 lb/sec is obtained. A larger model for the Douglas C-47 holds 1400 lb of bait, and the single hopper walls have narrow horizontal slits.[11] For satisfactory operation such hoppers must be closed at the top, and the emission pipe protrudes below the fuselage, being cut off obliquely to face rearwards. However, certain early models of suction hoppers developed for dusting have now been abandoned.[32]

Aerosol generators for aircraft

Exhaust Venturi tubes for producing aerosols of DDT in oil for mosquito control have been installed in the L-4, PT-17, Navy TBM, and C-47 aircraft. The exhaust gases are first piped some distance back from the engine in order to cool them before they pass through the Venturi tube, for otherwise the oil solvent would be completely volatilized. In the N2S Stearman the exhaust is carried 6 ft beyond the rear cockpit, where a Venturi tube is inserted with a constriction into which the DDT solution is injected.[51]

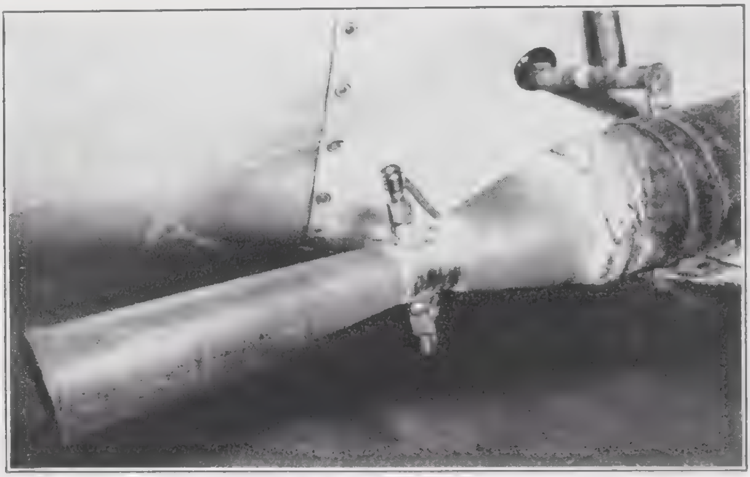

FIG. 7. Venturi section of exhaust aerosol generator mounted on the BT-13 Vultee aircraft. (Courtesy of Tennessee Valley Authority)

The Venturi tube contains a constriction whose diameter is from 2 to 4 in. (one-quarter to one-half the diameter of the exhaust stack in the Stearman PT-17) and whose length is 1.5 in. The entrance cone leading to it has an included angle of 20–30°; and the exit cone an included angle of 7° (Fig. 7). Two opposed flat nozzles spray the liquid into the constriction at a pressure of 50–80 psi. The solution usually employed is 20% DDT in a polymethylnaphthalene (e.g. *Velsicol*) solvent. The droplet size is decreased by narrowing the Venturi throat, which imparts a greater velocity to the exhaust gases, and is increased by injecting the spray liquid at a faster rate. The empirical relationship has been determined for these aerosol Venturi tubes as follows:[51]

$$\text{Mass median diameter (in microns)} = \frac{Q_F \times 10^7}{A_T \times V_T^2} - 3.66$$

where Q_F = volume of fluid injected (in cubic feet per second).
A_T = area of throat (in square feet).
V_T = velocity of exhaust gas in throat (in cubic feet per second).

In instances where the constricted Venturi tube causes too high a back-pressure and too fine an atomization, a "fishtail stack" without a constriction but with a terminal flat flare may be substituted. However, it is not considered desirable to install these generators on large aircraft.

The most effective aerosols for adult mosquito control have about 25% of their volume in droplets between 5 and 25 μ in diameter, smaller ones failing to contact the insects, and larger droplets being wasteful. More modern Venturi design introduces a coaxial feed which preheats the solution so that nozzles become unnecessary for atomization, and thus the stoppages caused by their clogging or coking are avoided.[99] The swath widths are reported to range between 33 yd for the Stearman exhaust Venturi and 100 yd for the C-47 fishtail stack.[100]

Helicopters

The helicopter, with motive power supplied by the main rotor and stabilized by a small tail rotor, has supplanted the autogyro (which is a conventional aircraft with a rotor replacing the wings) by virtue of its superior flying qualities. Tests made shortly before World War II showed that the autogyro had the advantage in manoeuvrability and landing over fixed-wing aircraft,[72] while at the same time it could carry as much as 750 lb of insecticide.[33] Present-day helicopters, although their load capacity is considerably less, are being adopted for aerial application in regions where the fields are small, e.g. The United Kingdom and eastern United States. The helicopter is not impeded by navigational hazards (such as trees, telephone and power lines, houses, and barns) which prevent fixed-wing aircraft from flying low enough to make a thorough treatment. Moreover the rotor downwash ensures that there is minimal drift of materials to adjoining fields. It must, however, be stated that helicopter

treatment of such small fields is expensive, and the coverage of sheltered corners by hovering or backing is hazardous for the machine and pilot, since once forward velocity is cut the helicopter loses lift and cannot turn without danger. Helicopters with their clear plastic noses allow the pilot to have full vision of the spray or dust application.[96] He also is enabled to modify his speed at will, which, however, may be a disadvantage if he does not remember that reduced speed increases dosage if the emission rate is not simultaneously reduced.

One of the great practical advantages of the helicopter is that it can land very close to the field it is treating, requiring no runway but only 15 yd of clear level ground. Thus the ground crew is almost continuously in communication with the pilot. Another, more important advantage is that a minimum of time is lost in ferrying. It has been claimed that, whereas fixed-wing aircraft spend only 20% of their flying time in making actual treatment, the helicopter spends 80% of its time in application.[49] Although this is not a true average picture, nevertheless a helicopter will treat a small (80-acre) area quicker than a Piper Cub, because of its superiority in the ratio of treatment time to flying time.[101] However, for areas approaching a square mile a helicopter is definitely inferior to a Stearman, not only because the fixed-wing plane is faster, carries a larger load, and gives a greater swath width, but also because so much time must be devoted to service and repair of the high-maintenance helicopter during large projects (see Table 3).

TABLE 3. Comparison of Helicopter (HNS-1) with Aeroplane for Time Consumption in Spraying Operations[101]

	85-Acre Area		575-Acre Area	
Time Consumed in:	Helicopter	Cub L-4	Helicopter	Stearman N2S
Ferrying	54	92	78	58
Spraying	62	58	103	79
Repairs and service	2	0	127	21
Total time, min	118	150	308	158

Another advantage of the helicopter is that the main rotor creates a strong downwash of air; the Bell model 47D moves

almost 2 million ft^3/min downwards at a rate of 12 mi/hr.[19] Insecticidal dusts are carried down with such velocity that they rebound to cover the undersurfaces of the foliage. When emitted from an altitude of 30 ft above orchards the dust cloud may be observed to rebound to a height of 20 ft. Sprays also may be made to rebound, provided they are located in the correct position with respect to the rotor.[73] Even with the weaker downdraft of a fixed-wing biplane (Navy N3N), 7% of the droplets from a coarse aqueous spray rebound to hit the undersurface of glass slides placed up to 14 in. above the ground.[98] The rotor downwash also enables dusting to be continued, without danger of drift, even if winds rise to 20 mi/hr; and without danger of upward dissipation, until the late morning and up to a ground temperature of 100° F. The downwash is also the best means yet known of forcing aerosols of DDT into forest cover to kill flying mosquitoes and blackflies. However, proper advantage of the downdraft may be obtained only if the forward speed is less than 12 mi/hr, the optimum (for width of swath) being 6–8 mi/hr.[73] When the speed is raised to 15 mi/hr the downdraft hits the ground 30–70 yd behind the machine when it is flown at the normal 5- to 10-ft altitude,[101] with a consequent upward loss of dust when field crops are concerned.[1] However, orchards with their higher crown cover may be dusted at 25 mi/hr, and emission may be maintained on turns. At speeds above 30 mi/hr and up to the maximum of 80 mi/hr, the translational lift changes the form of the downdraft until it more nearly resembles that of the fixed-wing plane.[1]

Thus the helicopter operator cannot increase his speed of application without sacrificing thoroughness. The necessary low speed becomes a handicap from the cost standpoint where larger areas are concerned. When this is coupled with the low capacity of helicopters (150 lb maximum for the HNS-1, 300–400 lb for the Bell 47, 250 lb for the Sikorsky YR4B), it becomes evident that the helicopter is at a disadvantage as compared to a biplane. However, the low capacity of helicopters may be only a temporary characteristic. When the helicopter was compared with the light airplane for the degree of control of cabbage loopers with 1% DDT dust on broccoli, it was found to be slightly (but insignificantly) inferior, even when application was at 16-yd in-

tervals from the helicopter and 20-yd intervals from the airplane.[73] In addition to the high maintenance requirements of the helicopter, its initial cost is high, being approximately 8 times that of a light fixed-wing aircraft.

Duster. The equipment of the Bell Model 47D consists of a pair of conical hoppers held on either side of the fuselage like panniers, each with a capacity of 200 lb, and agitated by a beater driven by an electric motor. Emission below the slide gate is aided by a jet of air borrowed from the air-cooling system of the rotor engine.[74] The width of swath when the dust is applied in still air from 6-ft altitude is 20 yd,[19] plus 3 yd of light deposit on either side. However, the binary origin of the dust cloud is betrayed by a bimodal deposit even in orchard dusting, and the effective swath width is closer to 15 yd. At low flying levels, the main rotor imparts to the dust a distinct throw to port.

Sprayer. The Bell helicopter may be adapted for spraying by the attachment of booms to protrude on either side of the fuselage at an angle of 15° with the horizontal, and by using the dust panniers as spray tanks. Pressure is applied by a centrifugal pump (40 psi, 30 gpm) with a power take-off from the main rotor.[74] A swath width of 13 yd may be obtained with the 8-ft booms. With the HNS-1 helicopter, emission from 30-ft height gives effective swath widths of 20–40 yd.[101] When the helicopter is flown 3–6 ft above the vegetation, 90% of the amount emitted may be recovered on the target.[57a] Experiments to decide the optimum position of spray booms with respect to the rotor of the Sikorsky YR4B revealed that they should be parallel with the rotor circumference and 1 ft within it; and that they should be located to the front of the machine, with the optimum position at an angle of 30° with the direct front. In the vertical plane, the boom gives best results when placed level with the fuselage floor, where it is also most convenient; for if it is raised to within 4 ft of the rotor, the spray is thrown directly outwards by the vortex at the rotor tip. The slipstream of a helicopter (with low forward velocity) is bell-shaped, the centre being calm; on reaching the ground it flattens out and then dissipates in rebound turbulence. The optimal height for boom and helicopter above the ground is 5–6 ft; if lower, no rebound occurs; if higher, there is loss of spray before the ground is reached.[73] The results are

satisfactory if the boom is 9 ft in front of the cockpit. In consequence of these experiments, the Cierva three-rotored Air Horse of 3- to 4-ton capacity is to be fitted with a single boom which skirts the base of the two forward rotors; the machine has already been dubbed the Spraying Mantis.

Aerosol generator. The Bell 47 helicopter may be fitted with a pair of Todd fogheads which are heated by the inverted exhaust of the main rotor engine. Concentrated solutions of DDT in oil are pumped to them from the side tanks at a pressure of 16 psi. If a wet fog of 10- to 40-μ droplet diameter is desired, the concentrate is delivered at 35 gph. Increase of delivery rate in the range 40–80 gph will give sprays of increasing coarseness.[71] When the helicopter is flown at 15 mi/hr 10 ft above the treetops, it throws down a swath of wet fog whose width is 70–100 yd (Fig. 8). This is an extremely effective method of control for blackflies and mosquitoes.

FIG. 8. DDT aerosols applied by the Bell 47 helicopter to control blackflies in the Adirondack region. (Courtesy of Bell Aircraft Corp.)

Physics of aircraft dusting

Dusts released from aircraft are highly sensitive to meteorological conditions. Because of the danger of vertical dissipation

and horizontal drift, they cannot be applied to crops at wind speeds in excess of 3 mi/hr[34] or under conditions of upward convection from the ground. As a consequence, crop-dusting operations are limited to 2 hr at sunrise and 1 hr at sunset.[6]

The apparent lightness of dusts is due not only to the small size of the particles, but also to their angularity. The settling rate may be increased by the substitution of more compact particles such as Celite (diatomaceous earth) or by coating the particles with oil.[10] The lightness and rigidity of dust particles prevent their impinging on vegetation, and thus crosswind dusting, as originally practised in 1921,[34] cannot be effectively applied. The addition of oil will increase the ability of a dust to impinge, but unless it is a drying oil (e.g. fish oil) it will volatilize and leave the dust particles to be washed off by rain.[72] Aircraft dusts are usually applied when there is dew on the crop to increase their adherence.

Field crops are dusted by aircraft flying as close to the ground as possible, i.e. an average of 5 ft from it or from the crop.[34] Consequently the swath widths are very narrow, measuring from 10 to 15 yd. The fall of particles is aided by the downdraft produced by the lower wing of a biplane (which in the Stearman 4-DX moves at approximately 600 ft/min[54]) or by the main rotor of a helicopter (which in the Bell 47D is 1100 ft/min or 12 mi/hr[19]). High-wing monoplanes such as the Piper Cub are unsatisfactory because their downdraft is weak, nor are they heavy enough to create sufficient air turbulence for the dust to penetrate foliage or superstable ground air layers.[10] The propeller slipstream and the wing vortices increase the swath width,[1,20] but they enhance the loss by drift. This is corrected to a greater or less degree by the downdraft of the wings, which also decreases the swath width. It is possible that the controllable swath width may be increased by using a pair of Venturi spreaders in a twin-engine plane[1] or by the use of wing vents in single-engine aircraft.[55]

For orchard work, the aircraft duster is flown 15–30 ft above the trees, and the resultant swath width is 13–23 yd.[6,11] For forest insect control, light aircraft are flown about 40–50 ft above the treetops, and the swath width varies from 33 to 50 yd

at the crown level, spreading to 70–100 yd on the forest floor.[84] Investigation of the deposit of a calcium arsenite dust in a forest of Scots pine showed that no more than 14% of the output was retained in the crowns of the trees. On the one hand, the dust particles greater than 74 μ in diameter penetrated to the forest floor; on the other, the particles of less than 53-μ diameter were lost by dissipation in the air. Of the fraction deposited on the foliage, only one-third was effective against *Panolis flammea*, since particles of over 61-μ diameter were too large to be ingested by the larvae.[2] When dust is emitted from a hopper in a flying aircraft it may acquire a static electrical charge, although this effect is not always observed. In a case where the crowns of coniferous forest carried a negative charge of electricity, it was found that emission of calcium arsenate dust with a positive charge ensured its adherence to the needles.[62]

The Huff-Deland-5 biplane, early developed for dusting of cotton and sugar cane, was able to achieve a swath width of 70–80 yd when flying at heights up to 25 ft. Russian biplanes applying calcium arsenite from heights of 33–40 ft achieved a swath width of 110 yd, but the edges of the swath were too lightly covered to kill migratory locusts. When these aircraft were employed to dust Paris green over water surfaces for malaria control, they obtained swath widths measuring between 110 and 200 yd from heights between 13 and 50 ft.[41,75] Paris green larviciding in the United States and Italy has been conducted at 65- to 200-ft altitude in calm weather, and 25- to 65-ft in winds ranging up to 12 mi hr.[18] Operations in Indo-China obtained a 220-yd swath width from flying heights of 100 ft.[41] Closer investigation of standard Paris green dusts applied from aircraft flying at 25-ft altitude under calm conditions revealed that only 20% of the amount emitted was deposited in the central 33-yd cross section of the swath, and that only 8% more could be found 33 yd on either side of it. The remainder, comprising approximately three-quarters of the dust load, was lost by drift.[illegible] Since *Anopheles* larvae can ingest particles up to 100 μ in diameter, a coarser dust was substituted. With this material, 84% of whose weight was in particles of 20–50 μ as compared with 18% for the standard dust, the amount deposited

on the water surface was increased to at least 60% of that emitted.[60]

The swath width and deposition of dust from aircraft may be determined by exposing plates coated with glycerine or Vaseline; the material deposited may then be analysed chemically. In cases where the aircraft flies high enough to avoid producing air turbulence at the ground level, the deposits may be caught in 6-in. Petri dishes or shallow crystallizing dishes and determined gravimetrically.

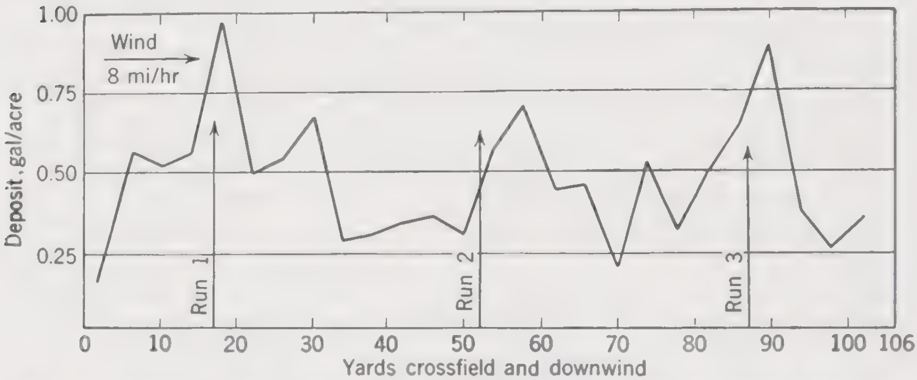

FIG. 9. Deposit of oil spray in wheat field by boom-and-nozzle assembly on the Lysander aircraft; meteorological conditions, high overcast sky in mid-afternoon.

Physics of aircraft spraying

The width of the swath of deposit produced by aircraft fitted with boom and nozzles and flying at minimal height is considerably greater than the length of the boom. The swath width from a Stearman biplane carrying a 26-ft boom and flying at 6-ft altitude is about 40 yd. On the other hand a Piper Cub with a shorter boom gave an effective swath width (against corn borer) of only 13 yd.[46] In the former case the boom extended far enough to deliver the spray into the wing-tip vortex, which widens the swath considerably but in an erratic manner. An increase in flying altitude results in a wider swath, owing to the combined action of the natural horizontal turbulence, the turbulence produced by the plane's passage, and the movement of the wind. If the wind is a factor, the downwind edge of the swath naturally

is composed of the finer droplets. Lateral displacement of the swath due to airscrew torque is considerable with high-wing monoplanes, but not with biplanes. Excellent coverage may be obtained by boom and nozzle aircraft flown in uniform strips at minimal height. The deposits obtained by a Lysander aircraft flying at 35-yd track intervals are plotted in Fig. 9.

Boom and nozzle assemblies with oil sprays give droplets ranging in size from the infinitesimally small up to 350 μ in diameter. For agricultural spraying, droplets from 50 to 300 μ in diameter are most commonly found in the spray discharge, with the recommended average about 180 μ.[1] A typical installation in the Piper Cub gave a spray in which 52% of the droplets were between 100 and 200 μ in diameter, and 84% between 50 and 250 μ. A more complete characterization of the spray, showing what might by analogy be called the "droplet spectrum," is displayed in Table 4. It may be seen that the droplets are most numerous in

TABLE 4. Droplet Sizes of Oil Spray Emitted from Fern-type Nozzles at 45 psi on a Boom on the Stinson L-5 Aircraft[77]

	Per Cent of Droplets in Each Size Class	
Size Class, μ	By Number	By Mass
10–40	8.0	0.14
41–100	41.0	7.2
101–160	32.0	27.2
161–220	15.0	35.9
221–280	2.0	10.7
281–340	2.0	18.5

the 40- to 100-μ size class, which comprises 41% of the total number of droplets. On the other hand the greatest proportion of mass or volume of the spray is contained in the 160- to 200-μ class, which comprises 36% of the total volume emitted (Fig. 10). The importance of the larger droplets is demonstrated by the following consideration: whereas only 2% of the droplets are over 280 μ in diameter, they constitute over 18% of the spray volume, yet the 41% of the droplets in the 40- to 100-μ class constitute only 7% of the total volume.

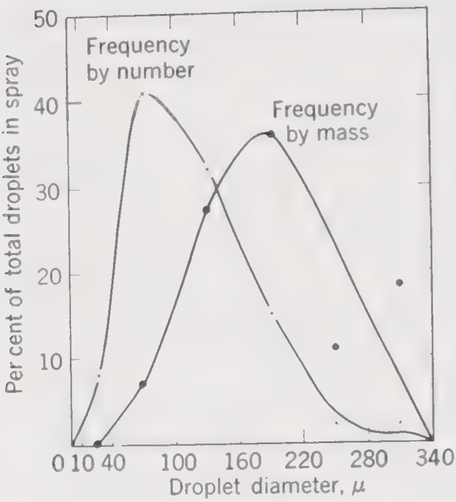

FIG. 10. Frequency distribution of droplet sizes in spray from aircraft fitted with fern-type nozzles. (Data from Sebora *et al.*, Table 4)

Since a single average figure is needed to characterize a given spray as to droplet size, it must be chosen with the main mass in mind. Neither the arithmetic mean, nor the median diameter by number, is satisfactory, since it fails to bring out the over-riding importance of the larger droplets. The best single figure is the median diameter by mass (mass median diameter, m.m.d.) which is the figure which divides the total volume of the spray into two equal parts. One-half of the mass of the spray is contained in droplets of smaller diameter than the m.m.d., and the other half is contained in droplets of larger diameter. The value of the m.m.d. may be determined by computing the volume in each size class and plotting the cumulative figures on logarithm-probability paper. When this is done for the figures in Table 4, the straight line obtained indicates the mass median diameter to be 185 μ (Fig. 11), as compared with the number median diameter of 98 μ.

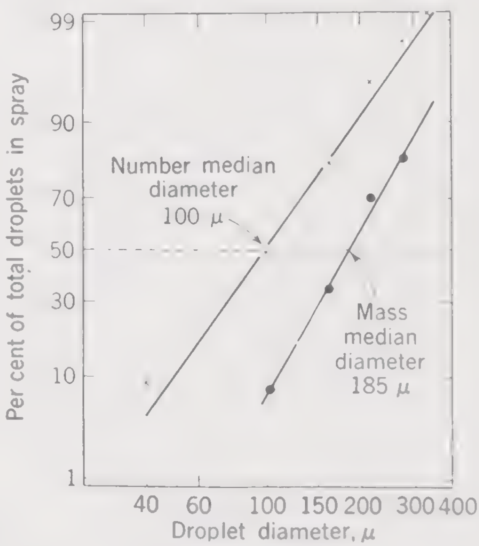

FIG. 11. Cumulative frequency distribution of droplet sizes in spray, derived from data of Fig. 10.

Oil sprays now used in mosquito larviciding are usually finer. The pumps employed for oil solutions develop pressures up to 150 psi; the droplet spectra obtained with various nozzles mounted on a boom carried

by a helicopter are shown in Table 5. However, the wettable powder suspensions generally employed for agricultural work are atomized at pressures in the neighbourhood of 40 psi, which is the limit for centrifugal pumps.

TABLE 5. DROPLET SPECTRA OF OIL SPRAY EMITTED FROM A BOOM AND VARIOUS NOZZLE TYPES ON THE HNS-1 HELICOPTER [101]

Size Class, μ	Per Cent of Droplets (by Number) in Each Size Class: Fern Type 55	Hollow Cone Bean 52	Solid Cone GG2 *	Flat Spray TT 8001
10–40	..	3	19	40
41–80	4	38	25	44
81–120	13	25	24	11
121–160	15	13	12	5
161–200	35	8	3	..
Over 200	33	13	17	..

* Pressure 125 psi, the others 150 psi.

The Porton method of spraying

The development of spraying equipment for light commercial planes has concentrated on obtaining an initial width of swath as the spray leaves the plane, mainly by the use of wide horizontal booms. To this extent the aircraft is being treated like a ground sprayer, and in character it is flown as close to the surface of the ground as possible. Yet even under those conditions the swath may be 5 times as wide as the spray equipment, and is even wider when the aircraft is flown at higher altitudes. The logical extension of this consideration is to apply from even greater heights and to emit from a point source below the fuselage. The wind operating on the spray as it falls will produce the swath width.

This principle, known as the Porton method [37] since it has been developed at the Experimental Stations at Porton, England (and Suffield, Canada), allows effective swath widths measuring up to 200 yd to be obtained. It is thus adapted to situations where large areas have to be covered, as in mosquito, locust, or forest insect control, and where a certain unevenness of deposit is not a serious drawback. The use of a point source eliminates the

need for booms. Since large aircraft such as the Douglas C-47 are used, the air speed is fast enough to give atomization without nozzles or hydraulic pressure. The spray liquid may be simply emitted from an open pipe into the region of relatively still air below the slipstream, where it is shattered because of the forward velocity with which it hits the air. The degree of atomization depends not only on the viscosity of the liquid at the time, but also on the rate of volume flow at which it is released. Forward speeds of 150 mi/hr are sufficient to shatter oils like kerosene or fuel oil into a fairly coarse spray, whose droplets show a median diameter by mass between 300 and 350 μ, and by number between 150 and 200 μ, and which range in diameter from below 10 μ up to 1 mm or slightly more (see Table 2).

TABLE 6. THE FALL OF WATER DROPLETS THROUGH AIR [10]

Droplet Diameter, μ	Character of Droplet in Nature	Terminal Velocity, ft/min	Time to Fall 100 ft, min	Distance Carried by 3-mi/hr Wind, yd
5	Sea fog	0.15	675	6000
33	Cloud	6.46	15.5	1360
100	Mist	55	1.82	160
170	(Fine spray) *	120	0.83	73
200	Drizzle	142	0.70	62
290	(Medium spray) *	229	0.44	38
380	(Coarse spray) *	313	0.32	28
500	Light rain	421	0.26	23
1000	Moderate rain	763	0.18	16
Free fall	....	1524	0.13	..

* Aqueous sprays atomized at 1000, 400, and 200 psi, respectively.

When this assortment of droplets constituting the spray is released into the air, it begins to fall and accelerates under the influence of gravity. But the viscosity of the air through which the droplets fall sets a limit on the maximum speed they can attain, which becomes their constant rate of fall or terminal velocity. The terminal velocity which a droplet can attain is decided by the ratio of its surface area (exposed to the viscosity of the air) to its volume; thus its size is an index of the terminal velocity at which it will fall through air. The larger the droplet, the

closer its velocity will approach the figure where the operation of gravity is not limited by the presence of air, a condition known as "free fall." The fall of droplets through gases or liquids which flow around them in a viscous manner is characterized by Stokes' law. Derivation of this law states that the rate of fall of small spherical droplets of water, in feet per minute, at 68° F is equivalent to $0.00593d^2$, where d is the droplet diameter in microns.[10] The terminal velocities attained by water droplets of various sizes are shown in Table 6, along with the consequent times they take to fall 100 ft.

TABLE 7. Deposit of Spray Downwind of Emission Track [26]

Distance Downwind, yd	Deposit Density, gal/acre	Droplets per sq dm, number	Median Diameter by Mass of Droplet, μ
30	0.05	15	440
50	0.8	950	310
80	1.3	810	305
100	0.4	1270	240
150	0.2	1180	180
200	0.2	560	185
250	0.1	320	100
300	0.05	380	100
400	0.05	62	55
500	Trace	145	40
600	Trace	94	30

Thus, when a spray containing a mixture of various droplet sizes is emitted into a crosswind, the largest droplets, which fall fastest, will be deposited closest to the aircraft track, and the smaller droplets will be deposited at greater distances downwind from the aircraft track. The distances the droplets are carried, and thus the characteristics of the swath, are proportional to the product of the speed of the crosswind and the height from which the droplets fall (see Table 6, columns 5 and 4). Thus it is found that the swath produced in a 10-mi/hr crosswind from a plane flying 50 ft above the ground is approximately equivalent to one obtained from 100-ft altitude in a 5-mi/hr crosswind; in both cases the height-wind product is identical, i.e. 500. This HV product, which is expressed in units of ft-mi/hr, may be calculated for any direction of the wind with respect to the direction

of flight. The crosswind component U of any wind may be calculated by multiplying the speed of the wind by the cosine of the angle θ by which it diverges from the crosswind. The crosswind component of a quartering 10-mi/hr wind is 7.07 mi/hr (i.e 10 cos 45°); when θ is 60° (the wind more on-track than crosstrack) the component is 5.0 mi/hr, and when it is 30°, the crosswind component is 8.7 mi/hr.

When the aircraft is flown at a height-wind product of 900 ft-mi/hr ($H = 120$ ft; $U = 8 \cos 20° = 7.5$ mi/hr), an oil spray of 220-μ mass median diameter deposits its largest droplets 30 yd downwind of the track. The heaviest deposit is 80 yd downwind of the track, where the droplets are about 300 μ in diameter. The deposited droplets are most numerous 20 yd further downwind (see Table 7). A plot of the deposit for 750 yd of flight is shown in Fig. 12. It shows that the deposit continues to exceed 0.25 gal/acre (when emission is at the rate of 3.4 gal per 100 yd of flight) for a distance of 200 yd downwind. The proportion of spray deposited on the ground to that emitted from the aircraft was 65% in this case. The effective swath width may be increased above 200 yd simply by increasing the emission rate or decreasing the speed of the aircraft.

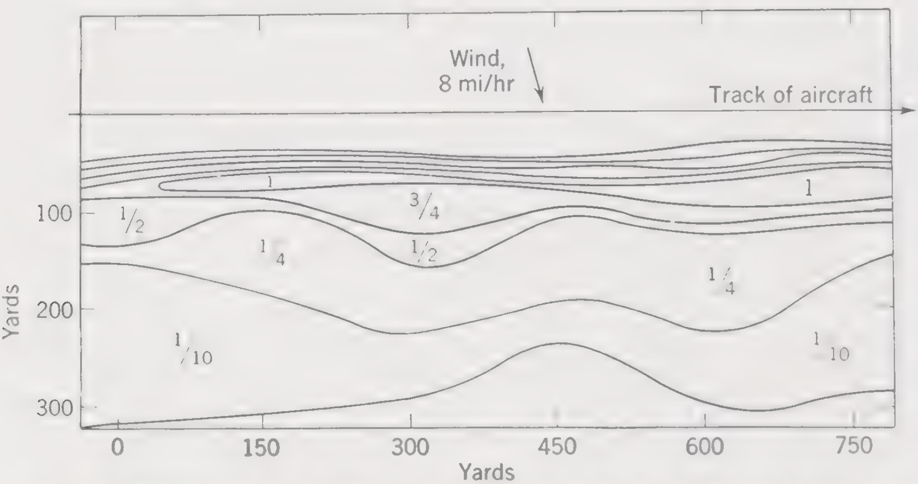

Fig. 12. Single swath of deposit, in gallons per acre, of oil spray (from the B-25J Mitchell III aircraft flying crosswind). Mixture of 9 parts fuel oil with 1 part *Velsicol* solvent (viscosity, 2.5 cp at 25° C). Airspeed, 210 mi/hr (105 yd/sec); emission rate, 3.6 gal/sec (3.4 gal/100 yd); height, 120 ft; height-wind product, 900 ft-mi/hr.

When a large area is to be sprayed, parallel runs are made at intervals dictated by the density of deposit to be obtained. Then application is made from such a height that the height-wind product is large enough, and the swaths therefore wide enough, to overlap. Nearly always enough crosswind component will be found in the wind obtaining at the time, though this method is not to be recommended if the wind is less than 15° angular distance from the track ($\cos 75° = 0.26$). The height of the aircraft is increased to give the HU product desired, the relatively stable atmospheric conditions ensuring no interference with the fall of spray, until a height is reached where the small droplets are lost by volatilization; for kerosene or fuel-oil sprays this height is about 500 ft.

Track of aircraft 70'

Wind, 17 mi/hr

Yards	40	240	440	640		840 880
10	0.11	0.69	0.20	0.90	70'	0.57
20	0.15	0.46	0.76	0.59		0.24
30	0.16	0.81	1.09	1.10		0.62
40	0.36	0.46	1.45	0.37		0.26
50	1.18	0.34	1.40	0.64		0.40
60	0.33	0.82	1.04	0.68	60'	0.25
70	0.28	0.24	0.58	0.72		0.57
80	0.30	1.33	0.50	0.24		0.32
90	0.77	0.43	1.29	0.28		0.41
100	0.53	1.04	0.31	0.50		0.48
10	0.40	0.97	0.51	0.59	80'	0.43
20	0.43	0.56	0.28	0.38		0.43
30	0.11	0.66	0.31	0.90		1.10
40	0.12	0.24	0.17	0.87		0.44
50	0.20	0.44	0.15	0.32		0.47
60	0.25	0.53	0.62	0.72		0.98
70	0.49	0.39	0.09	1.17		0.39
80	0.32	0.37	0.76	0.70		0.44
90	0.43	0.38	0.46	0.54		0.33
200						

Boundary of field

FIG. 13. Four swaths of deposit of oil spray from the C-47 Dakota aircraft flying crosswind at 50-yd track intervals over a 36-acre wheat field. Longitudinal scale foreshortened 3 times for convenience. Deposit densities in pounds per acre of dissolved insecticide sampled every 10 yd on 5 cross-field lines; average deposit density, 0.57 lb/acre; flying heights, 60–80 ft.

The deposits obtained over a large field of mature wheat, 200 yd wide and 880 yd long, treated for grasshopper control by this method are plotted in Fig. 13. The application was made from

the Douglas C-47 aircraft in 4 runs at 50-yd intervals, the first run being upwind of the field. Since the heights were 60–80 ft above terrain, and the wind speed 15–19 mi/hr and its direction within 5–15° of crosstrack, the height-wind product was 1100 ft-mi/hr. Every point sampled on the field is well covered.[28] In Fig. 14 is shown a transect of 750 yd of locust-infested territory in Tanganyika,* which was treated by an Anson aircraft at an *HU* product of 2000 ft-mi/hr and strip intervals averaging 75 yd.[90] For mosquito control in Canada, a height-wind product of 1500 ft-mi/hr gives satisfactory coverage for 200-yd strip intervals.[89]

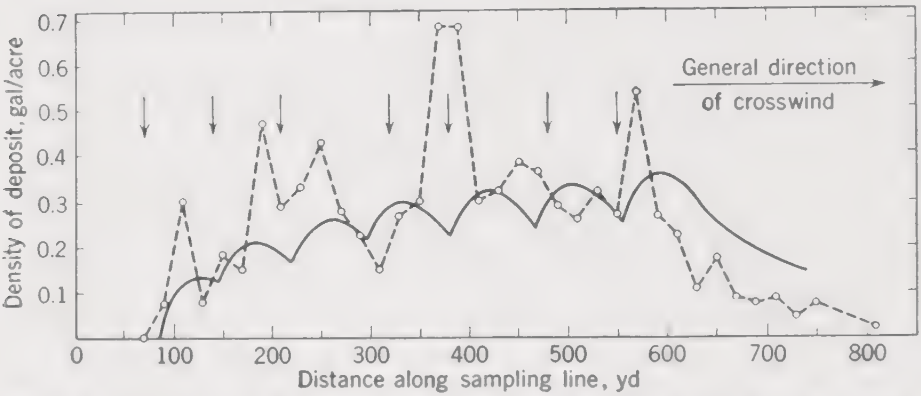

FIG. 14. Transect of 7 swaths of deposit of oil spray from the Mk. XIX Anson aircraft flying crosswind at 75-yd track intervals and at a height-wind product of 2000 ft-mi/hr. Solid line, expected deposit; dotted line, actual deposit in gallons per acre. Aircraft flights marked by arrows; the flight at 270-yd point omitted from the operation. (From Gunn *et al.*, 1948)

Oil-in-water emulsions, when applied by the Porton method, follow much the same pattern of fall as fuel-oil solutions, the greater density of water being counteracted by its greater evaporation during its passage through the air. Roadways infested with clear-winged grasshoppers have been accurately hit by emulsions emitted into a crosswind by allowing the same windage as for oil solutions.[11] It is probable that suspensions behave similarly, although the effectiveness of wettable powders in giving

* Physical aspects of the aerial curtain method of spraying locust swarms in flight have been discussed by Sawyer [*Bull. Ent. Res.*, **41**: 439–457 (1950)].

contact kill of insects such as locusts and mosquito adults is greatly inferior to that of solutions.

Physics of aircraft baiting

When oil-base bran bait is emitted from a dusting hopper in a light aircraft, the swath width is 7 yd when applied from a height of 15 ft, 16 yd from 30 ft, and 30 yd from 50 ft.[94] Baiting operations with Stearman 4E, White Standard, and other light aircraft in the United States are based on a 16-yd swath width.

Wider broadcasting of bait was obtained in the early work in Uzbekistan, the swath width averaging 27 yd and rising to 85 yd in a crosswind. From a height of 330 ft a swath width of 110 yd was attained.[66] Oil-base baits made with bran and sawdust, where 75% of the particles are between 10- and 40-mesh sieve size, show dispersal characteristics not greatly different from those of oil sprays when applied from the air. When a Norseman C-64 or Douglas C-47 is flown upwind at 70- to 100-ft attitude, emitting at a rate of 0.25 lb/yd of flight, the swath above 5 lb/acre is 30 yd wide, and above 0.25 lb/acre it is 50 yd wide. When these aircraft emit bait into a crosswind at a height-wind product of 1000 ft-mi/hr and an output of 0.25 lb/yd, the width of swath with deposits in excess of 5 lb/acre measures 55–90 yd, and above 0.25 lb/acre it is approximately 150 yd. Although the bait particles are larger than spray droplets, they are generally flatter and present more surface, and thus fall at roughly similar rates. Although the bran separates from the sawdust in its fall, the ratio of bran to sawdust remains unchanged, except for the upwind 40 yd where the deposit is composed of the large fragments of sawdust.[27] When a wheat field measuring 1 mi long by 130 yd wide was treated in a crosswind at a height-wind product of 600 ft-mi/hr and track intervals of 50 yd, a notably even deposit was obtained, comprising 74% of the amount of bait emitted, and it resulted in over 95% control of the grasshoppers infesting the field.[13]

Physics of aerosol application

The droplets of DDT concentrate used in the production of aerosols are heavier than oil- or water-spray droplets and thus settle more rapidly. Application of Stokes' law to droplets of

specific gravity 1.12 reveals that their terminal velocity in feet per minute is equivalent to $0.00675d^2$. Moreover, aerosols are emitted with the Venturi tube or foghead so placed that the downdraft of the lower wing imparts to them a velocity of 600 ft min, or the helicopter rotor a velocity of 1100 ft min. The fine aerosol droplets carried downward by this downdraft are much more effective in penetrating heavy vegetative cover than the coarser sprays falling by gravity.

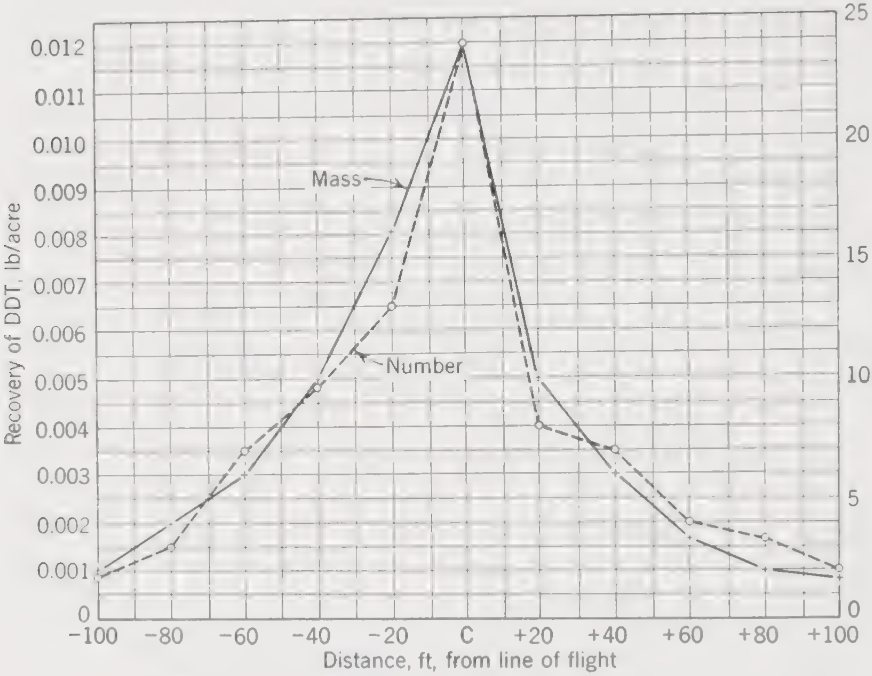

FIG. 15. Crosstrack distribution of deposit of aerosol, of m.m.d. 35–40 μ, from the PT-17 Stearman aircraft flying at 25-ft height in still air, and discharging at the rate of 0.1 lb DDT per acre. Recovery of mass in pounds of DDT per acre; recovery of number in drops per square centimetre. (From Kruse and Metcalf)

The swath produced with an aerosol of 35- to 40-μ mass median diameter, emitted from a height of 25 ft, is shown in Fig. 15. It may be seen that the deposit at a distance of 100 ft on either side is one-twelfth that at the centre.[31] The peak of deposit in the centre is mainly attributable to the large droplets. Droplets less than 25 μ in diameter extend well beyond the 100-ft limit. When the aerosol is emitted at such a rate that with flights

100 ft apart an expenditure of 0.2 lb/acre of DDT is applied, the effective swath width to kill *Anopheles* larvae is 240 ft (80 yd); for an expenditure of 0.05 lb/acre it is 180 ft (60 yd). If heavy vegetative cover overlies the water, these effective swath widths contract to 115 ft and 10 ft, respectively.

Despite low flying and the downdraft provided by the airplane, the percentage of material that is deposited on the water surface remains surprisingly low. With the 35-μ aerosol plotted in Fig. 15, the deposit over the 200-ft swath is 9% of the amount discharged.[54] The recoveries of DDT at ground or water level for aerosols of between 80- and 25-μ mass median diameter may range from 25% down to less than 5% of the amount emitted.[35] When aerosols of 35- to 40-μ m.m.d. were compared with aerial sprays of 75- to 100-μ m.m.d., for a given emission rate the aerosol spray deposited one-twelfth as much as the spray when emitted from 25-ft altitude; when the altitude of flight was 50 ft, the spray deposited 24 times as much insecticide as the aerosol.[19] Even when woodland pools are concerned, the deposits from the aerosol do not exceed one-quarter of that from a spray.[82]

The amount of aerosol deposited decreases with the air temperature prevailing, 2.5 times as much being deposited at 14° C as at 22° C. The deposit is increased when the density of the insecticidal solution is raised, substitution of a 1.12-sp. gr. liquid for one of 1.02 sp. gr. increasing the deposit approximately threefold.[19]

Meteorological conditions

Spray droplets present to the air the same outline throughout their entire descent, and thus their course may be predicted with sufficient certainty to aim them at a target from a height. Such predictions presuppose an absence of the vertical turbulence which moves air masses upwards from the ground, causes "air pockets," and will billow up a cloud of spray emitted into it. This upward convection is due to the warming of the earth to a temperature above the overlying air. It is superimposed upon, and distinct from, the horizontal movement of air which is known as wind. As every pilot knows, on clear days turbulence starts about 1 hr after sunrise and dies down about 1 hr before sunset. On cloudy days vertical turbulence may not appear, since the ground

surface is not sufficiently heated by solar radiation. Water surfaces do not heat rapidly enough to cause marked turbulence of the air above them at any time.

The degree of turbulence prevailing in the air may be determined on the ground by measurement of the temperature at two height levels, to ascertain whether the lower level is warmer than the upper. Although widely separated heights (for example 4 and 56 ft) are the most satisfactory, levels of 1 metre and 2 metres are adequate and convenient. If the upper level is warmer than the lower, there is a positive temperature gradient; since the cooler denser air underlies the warmer air the conditions are stable, a condition characterised as inversion. If the lower level is warmer than the upper, the temperature gradient being negative, the air tends to rise from the ground, a condition known as lapse, resulting in turbulence. Pronounced inversions, with high positive temperature gradients, can build up on calm clear nights; wind will reduce this inversion but not eliminate it. The point where the two temperatures become equal is known as zero gradient or "change-over."

The temperature gradient is measured by means of two thermocouples, mounted on a mast and shielded from the sun, connected to a sensitive galvanometer. If this apparatus is not available, it may be derived empirically from comparison of the wind speeds at an upper level with that at a lower level. At zero temperature gradient the ratio between the wind speed at 2 metres and that at 1 metre, the so-called wind ratio, is on the average 1.14. On a clear day under conditions of maximum lapse rate (high positive temperature gradient) the wind speeds are nearer to equality and the wind ratio falls to about 1.08. On clear calm nights under conditions of maximum inversion it may rise to 1.40. From use of the wind ratio, the vertical turbulence may be measured by the same anemometers that determine wind conditions in the field.[9]

Spraying procedure

In crop application it is good practice to post a flagman on the ground to mark the beginning of each emission track and to pace off the track intervals. He may be provided with a coloured flag or an Aldis lamp. Some crop dusters dispense with a flag-

man and judge their succeeding runs from the cloud remaining from the previous run. Every alternate run is made in the opposite direction, and each succeeding flight upwind of the previous one. It is, however, the general experience that a ground man is almost essential, and a system of hand signals has been devised for him to communicate with the pilot.[70]

In large-scale spraying, such as forest insect, mosquito, or locust control, it is safest to emit while flying in one direction only, the markers being moved along a crosstrack starting line. With large aircraft the turning radius is so wide that tight turns for return runs are not profitable. The markers used have been smoke pots (whose spreading plume leads to inaccuracy), cloth panels with luminescent dye (excellent if obstructions are few), and hydrogen-filled balloons for forest work. A special balloon, resistant to puncture by trees, drift from wind, and bursting from lowered air pressure, has been developed in Germany; it is oval in shape, constructed of rubberized cotton, and provided with a special safety valve.[92] In areas completely impenetrable to a ground crew, but with good landmarks, the runs may be laid out from a map made from aerial photographs. With the larger aircraft it is possible to have ground-to-air radio communication. This is essential where the spraying procedure utilizes the crosswind, as in the Porton method; it is the function of the ground crew to ascertain wind speeds and directions and determine the desired heights of flight.

The dosage applied is decided by the emission rate, the speed of the aircraft, and the distance between tracks. Since the last two points are fixed by the characteristics of the plane and of the installation, the only adjustable feature is the emission rate. This bears a relation to the speed at which the aircraft covers the ground with spray; the spray coverage (in acres/min) is equivalent to:

$$\frac{\text{Track interval (in yd)} \times \text{Aircraft speed (in yd/min)}}{4840}$$

Then the required emission rate (in lb/min) is the product of the spray coverage (in acre/min) and the dosage required (in lb/acre). In the cases where it is not convenient to modify the volume of spray liquid emitted, the percentage of insecticide in the spray may be adjusted.

Sampling methods

The characteristics of the swath produced by a light plane fitted with boom and nozzles are readily ascertained by stretching a roll of paper (e.g. adding-machine tape) across the track. This paper may be treated with a chemical (e.g. haematoxylin), on which a characterizer compound added to the spray liquid (e.g. aluminum chloride) develops a coloured spot to mark each droplet. Or a surface may be treated with polyvinyl acetate and *p*-nitrobenzene-azo-β-naphthylamine in acetone; droplets falling on this golden coating appear as black circles.* The density of deposit reaching the ground may be determined by using dyed spray (e.g. Williams red, i.e. Dupont oil red or waxoline red for oils, Rhodamine B, croceine scarlet, potassium permanganate, or coloured inks[78] for water-base sprays) and placing 4-in. glass plates (e.g. Petri dishes) at appropriate intervals across the track. The deposit in the dish is colorimetrically assessed by washing it off with an aliquot of solvent and comparing it for colour density with the original spray liquid diluted by a known amount. A deposit of 7 mm^3 of spray in a 75-cm^2 Petri dish is equivalent to 1 gal/acre. This deposit, washed off with 5 cc of solvent and compared with a 1/1000 dilution of the spray liquid, will show a relative colour value of 7 over 5.

The droplet size may be determined by exposing glass plates coated with material that prevents their spreading on the surface, so that they remain as a partially flattened droplet standing up sufficiently to be sized. For aqueous droplets, coatings have been made with resin in castor oil, Gelva resin, and polyisobutylene.[58] At present aluminum stearate, mannitan monolaurate (*NNO*), and *Drifilm 9987* † are used as oleophobic coatings for the study of oil sprays; the last material, a silicone compound, is the most satisfactory. The droplet that has fallen on the coating spreads to form a lens whose diameter is determined by the final contact angle that its margins make with the coating.[58] For most spray liquids on the coatings commonly used, the ratio of the droplet diameter D to the lens diameter A, i.e.

* Check papers made to show droplets in colour are patented by and available from Independent Crop Dusting, Inc., Campbell, California.

† Available from the General Electric Company, Schenectady, New York.

the spread factor D/A, is between 0.25 and 0.60. Determination of the focal length f of the lens,* which is accomplished by placing it on the stage of a microscope and passing parallel beams of light through it, allows the derivation of the value of the contact angle θ from the equation

$$\frac{f}{A} = \frac{1}{2(\mu - 1)\sin\theta} + \frac{1}{2}\tan\frac{1}{2}\theta$$

where μ is the refractive index of the liquid in the lens. The value of the spread factor D/A may be derived from θ by reading off the curve in Fig. 16. For example, the spread factor of fuel-oil droplets on the *Drifilm 9987* silicone is 0.5; thus the diameter of the droplets is one-half the diameter of the lenses they produce.

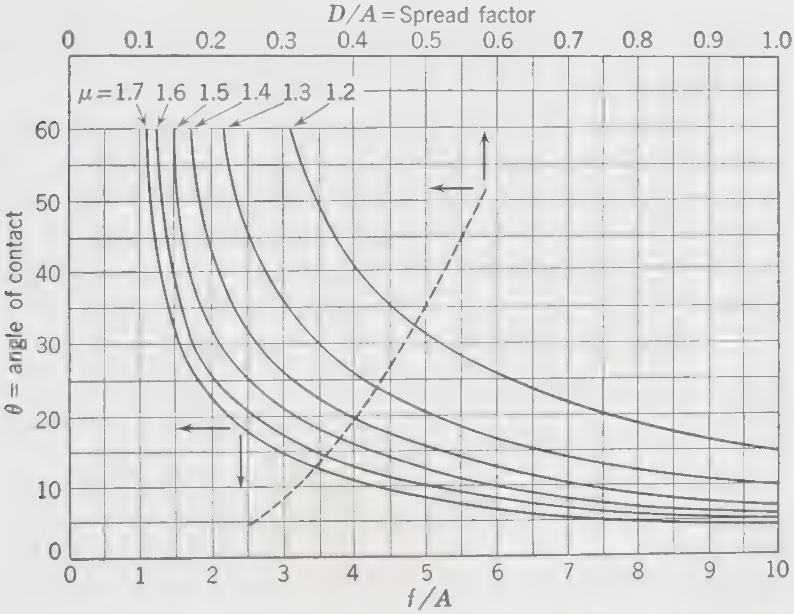

FIG. 16. Curves for computing the original drop diameter from the lens diameter. First, from the determined values of f/A and μ, read off the value of θ from the solid lines. Then, from the dotted line the spread factor, D/A, corresponding to θ may be obtained. (From May)

The droplet diameter may be measured directly by using glass plates smoked with a fluffy coating of carbon (e.g. lampblack [31])

* Distance of the focal point from the surface of the glass slide.

or magnesium oxide. Here the droplet punches a hole in the coating before spreading out on the glass underneath. With magnesium oxide, the hole is slightly larger than the drop, so that a correction factor of 0.85 has to be applied to the measured value (this is for droplets $>20\ \mu$; for $<15\ \mu$ the factor is 0.75). Or depression microscope slides may be used, containing an aqueous solution of glycerin, gelatin, oleic acid, and triethanolamine, into which the oil droplets fall and maintain their spherical shape.[43a] For trapping aqueous droplets, a mixture of mineral oil and petrolatum jelly is used.[58]

Measurements of droplet size are made under the microscope, using an ocular micrometer checked by a stage micrometer; if one or both is unavailable at the time a rough standard of comparison is provided by a human red blood corpuscle, which measures 7 μ in diameter. The most suitable ocular micrometer is Fairs' modification of the Patterson-Cawood graticule, or the so-called Porton model.*

On unsized papers of close texture, and on filter paper, droplets will spread to give a roughly circular stain. If these are measured before the edges become ragged, a rough idea of the droplet size may be obtained on the assumption that the spread factor is approximately 0.16, the stain being 6 times as wide as the droplet. The spread factor may be determined by blowing off small uniform droplets from the tip of a capillary microburette; the number of droplets falling on the paper is related to the microvolume delivered, and hence their true diameter can be computed from their individual volume. This is then compared to the diameter of the stain which they produce. The stains may be measured by illuminating magnifiers fitted with a micrometer.† From the sizes of the droplets and the number deposited per unit area, it is possible to calculate the area dosage. This replacement of the colorimetric method is useful when a colorimeter is not available.

Aerosols, which kill insects by air concentrations rather than area deposits, are more accurately determined by air-sampling

* Available from C. F. Casella and Co., Fitzroy Square, London, W 1

† For example, Luminex Illuminator, available from R. and J. Beck, London.

methods. The most useful piece of apparatus is the cascade impactor, into which air is sucked at 17.5 litres/min through an orifice measuring 19 by 7 mm, to impact the droplets on a glass microscope slide; those that are too small to impact at that speed are carried by a cascade system of 3 jets of successively smaller orifices to impact at successively higher speeds on 3 more glass slides, which catch droplets of 20-, 7-, and 3-μ diameter, respectively. The slides may be used to determine the product of the concentration of the aerosol and the time over which it operated; this value Ct is expressed in mg-min/m^3, and is a more useful figure than the concentration alone in mg/litre because it represents the amount of insecticide available to poison the insect. By the use of suitably coated slides inserted in the cascade impactor, the particle sizes may be determined by the methods outlined above.[58]

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C H A P T E R V I I

Toxicity and Hazards to Man and Domestic Animals

General considerations

Whereas it is the task of the pharmacologist to determine the toxicity of economic poisons by experiment, it has become the role of the public servant to establish their hazard on the basis of experience. Conditions of formulation, packaging, sale, and use may make a less toxic poison (e.g. sodium fluoride) more hazardous than a highly toxic one (e.g. TEPP).

The best general criterion for the acute toxicity of a solid or liquid compound is the median lethal dose (LD_{50}) by oral administration, determined on rats or other laboratory animals, and expressed in milligrams per kilogram of body weight (mg/kg). For a gaseous fumigant, the LD_{50} is best expressed as the vapour concentration in milligrams per litre multiplied by the duration of exposure, e.g. in milligram-minutes/litre. However, it is usually reported as the level in parts per million (ppm) which produces a given response in a certain time. The chronic toxicity is generally determined by feeding a given concentration in the entire diet, and determining the maximum level in parts per million which fails to induce symptoms or death.

The hazards involved may be classified as occurring in the manufacturing plant, in the home, in formulation and mixing, in field application, and finally in the consumption of contaminated

foods. Plant hazards are not the concern of the economic entomologist, but he may profit by learning their lessons. Hazards in the home include the ingestion of insecticides by mistake, particularly by children. Roach powders, ant syrups, and fly sprays are most commonly involved in these accidents. These dangers may be overcome by proper labelling, with the poison vignette and with the antidote specified, and by the use of bottles of characteristic shape. Powders containing fluorides or arsenicals may be dyed pink or some other warning colour. The hazards of formulation and mixing involve the raising of a cloud of the fine powder which is inhaled into the lungs, or licked from the lips, of the worker. Since many of the modern organic insecticides are formulated in petroleum oils and are themselves soluble in the skin oils, there is a danger of skin contamination. The first hazard is met by the wearing of a respirator, and the second by rubber gloves and coveralls, preferably treated with a protective impregnant. Working conditions constitute the most important factor in protection, and should include adequate room, good ventilation, and a moderate temperature. Provided the worker has plenty of time, he can be relied upon to take the necessary precautions, including the donning of protective clothing; if overheated, he may be tempted to remove respirator and clothing when safety requires that he should wear them.

In field application the most serious hazard is drenching of the spray operator because of vagaries in the wind or carelessness in operation. Often the sprayman will wear a rubberized "slicker" as the only protective clothing. Respirators are virtually never worn, although in some cases they are demanded by public safety organizations; their disadvantage is that they cut down the sprayman's general awareness of the environment. The best precautions are simplicity in clothes (which should be preferably one-piece, loose, and non-absorbent) and their immediate replacement if contaminated; also a careful observation of the wind drift, especially on gusty hot days. For field application of fumigants in buildings, respirators should always be worn. The appropriate canisters are important, since HCN, acid gases, chloropicrin, and organic phosphates each require their own special filling, which is different from the standard canister (GMA) for organic chlorides and esters. The suitability of the

canister filling for the particular vapour is verified by the U. S. Bureau of Mines approval.

The final hazard is the persistence of toxic residues on plant products until the time they are consumed. This is negligible in the case of volatile insecticides (e.g. nicotine, BHC, parathion) and labile compounds (pyrethrins, TEPP). It is considerable when the spray chemicals are absorbed into the plant tissue (e.g. parathion, systemic insecticides). The most dangerous compounds are the non-volatile inorganic poisons (arsenicals and fluorine compounds) and organic insecticides such as DDT and dieldrin. The toxicologist must determine their toxicity, decide whether they are cumulative or not, and establish whether they are excreted or stored in the tissues. Again DDT, itself only slightly toxic, presents a unique hazard in its tendency to concentrate in fatty tissue and secretions such as milk.

The search for ever more powerful insecticides leads to a point where a compromise has to be made between the insecticidal value and the hazard to warm-blooded animals. A balance has been struck in the case of HCN, one of the most poisonous gases, whereby it may be used as an insecticide provided the most stringent, state-enacted precautions are taken. Nevertheless victims are claimed by accidents every year. A similar situation is developing with the liquid parathion, the closest approach to a universal insecticide, but feared because of its mammalian toxicity. Perhaps here too a programme of education and legal regulation may strike a balance, once research has elucidated the precise hazards, so that this powerful weapon can be utilized. It is evident that pest control has unavoidable occupational hazards and requires financial insurance and rules of practice; at least the hazards are no higher than those normally encountered in the automobile and air age.

Fumigants

Hydrogen cyanide. Hydrocyanic acid gas, or HCN, is one of the most toxic vapours to higher animals. On being absorbed into the blood stream it is carried to the tissues, where it inactivates the cytochromes and cytochrome oxidase that are essential for cellular respiration. Since its odour is mild and sweet it gives no olfactory warning, nor has it any automatic mechanism

of reducing the respiratory intake. It acts rapidly, and concentrations above 3000 ppm are rapidly fatal. The lowest vapour concentration tolerable by mammals without symptoms developing is 16 ppm (0.02 mg/litre; cf. Table 1). Concentrations above 20 ppm are very dangerous if inhaled for more than an hour.[105, 113]

Hydrogen cyanide is readily absorbed by the skin. When applied to a 1-in. circle of epidermis it was found to kill guinea pigs within 8 min.[220] Men wearing respirators, but with their skin unprotected by special clothing, almost succumbed within 10 min of exposure to a vapour concentration of 20,000 ppm and were incapacitated for the following 3 days.[65]

The lethal dose of HCN taken orally is 50 mg for man[90] (equivalent to 0.8 mg/kg). Normally foods fumigated with this compound readily give up the adsorbed gas on removal to fresh air, but green vegetables have been found to absorb HCN.[96] It is considered that food contamination is tolerable so long as it does not exceed 75 ppm, a level that is normally found in bitter almonds.[186]

The symptoms engendered in man by a short exposure to sublethal concentrations of HCN are throat irritation, salivation, watering of the eyes, difficulty in breathing, and giddiness,[113] followed by headache and high pulse rate for several hours, and general weakness for some days. Exposure of laboratory animals to lethal concentrations results in their showing wild excitement and ataxia, followed by coma and respiratory paralysis; death may be immediately preceded by convulsions.[93, 225] There is no histopathology of tissues or organs, except for the appearance in some cases of bright red blood and pink "cyanide" lungs.

As an antidote, sodium nitrite, amyl nitrite, or methylene blue has prophylactic value[186] by converting the haemoglobin of the blood to methaemoglobin, which fixes the cyanide and thus prevents its reaching the tissues. Administration of sodium thiosulphate will then convert the cyanide into thiocyanate, in which form it can be excreted in the urine.[93]

Hydrogen sulphide. On the increasingly rare occasions on which it is used as a fumigant, H_2S presents few hazards because its offensive smell makes it self-warning. Its toxicity, however, almost rivals that of HCN,[105] 1000 ppm killing almost instantly,[illegible] and exposure to 200 ppm for 1 hr being dangerous. A vapour

concentration of 100 ppm is sufficient to irritate eyes, nose, and throat.[113] Hydrogen sulphide may be absorbed through the skin, but not as readily as HCN. It causes nervous symptoms, headache, vertigo, and nausea when sublethal, and violent activity and ataxia when lethal. Death is preceded by respiratory failure, and edema or haemorrhage will be found in the lungs.[220] As an antidote, oxygen and artificial respiration may prove effective.[93]

Sulphur dioxide. The toxicity of SO_2 is comparatively low. Laboratory animals can survive exposure to 1000 ppm for 24 hr [221] and can thrive in an environment containing 33 ppm. For man, a vapour concentration of 10 ppm is safe for continuous exposure. Sulphur dioxide is a self-warning gas, since at 20 ppm it causes weeping and coughing. Whereas an exposure to 500 ppm for 1 hr is considered dangerous, a concentration of 200 ppm is intolerable and will drive a man out if an exit is available.[113]

Mild symptoms in human beings include nasopharyngitis, shortness of breath, increased fatigue, abnormal reflexes, and a change in taste and smell sensations.[119] More severe symptoms in man and animals include throat inflammation, lung edema, and paralysis of the hind quarters. Post-mortem examination of severely poisoned animals reveals haemorrhage of lung and stomach, dilatation of the heart, and distension of the gall bladder.[224]

Carbon disulphide. Although its commercial preparations are mildly offensive in smell, CS_2 is not self-warning. The vapour concentration below which continuous exposure is safe is set by some at 10 ppm,[95] by others at 3.3 ppm (0.01 mg/litre). Symptoms may appear in man on daily exposure to 33 ppm or single exposure for a few hours to 330 ppm. This fumigant is liable to be absorbed through the skin.[147]

Carbon disulphide, being liposoluble, is a nerve poison. Initial symptoms include headache, irritability, wavy vision, and mental confusion, and may be followed by cramps, stomach trouble, and nightmares.[93] Prolonged exposure to sublethal concentrations results in drowsiness, anemia, asthenia, hysterical outbursts, and general debility, which may lead to sexual impotence and dementia.[113] Exposure to high concentrations above 1000 ppm for

not less than 30 min may lead to excitement, impaired vision, coma, convulsions, and death by respiratory failure.[93]

Chloropicrin. This tear gas is highly poisonous and has been used in chemical warfare. The LD_{50} of the vapour for dogs is 120 ppm (0.8 mg/litre) for 30 min, and the maximum concentration tolerable by animals for 1 hr without serious symptoms appearing is 1.0 ppm (0.007 mg/litre).[113] Fortunately chloropicrin is self-warning, being detectable at 1.25, lachrymatory at 2.4, a throat irritant at 11, and a sternutant at 17 ppm.[235] The irritation of the alveolar walls of the lung results in an edema which may prove fatal, but from which permanent recovery is possible.

TABLE 1. Toxicity Hazards of Fumigants and Solvents [113]

Material	Maximum Tolerable Concentration,* For 60 min mg/litre	Maximum Tolerable Concentration,* For 8 hr mg/litre	Probable Safe Concentration † for Indefinite Exposure mg/litre	Probable Safe Concentration † for Indefinite Exposure ppm
Chloropicrin	0.007	....	....	...
Hydrogen cyanide	0.05	0.02	...	...
Sulphur dioxide	0.13	0.02	....	....
Dichloroethyl ether	0.22	0.15	0.10	15
Hydrogen sulphide	0.24	0.10	....	....
Carbon disulphide	1.5	1.0	0.01	3.2
Methyl bromide	3.9	0.19	0.05	100
Ethylene oxide	5.4	0.45	0.45	250
Ethylene dichloride	10.2	2.9	0.43	100
Methyl formate	10.9	3.3	3.7	1500
Carbon tetrachloride	60	10	0.69	100
Benzene, toluene, xylene	10	5	0.34–0.48	100
Turpentine	......	.....	4.0	700
Gasoline	......	.....	4.0	1000

* Tolerable without serious, but only slight, symptoms; based on guinea pigs.

† ppm = mg/litre × 24,450/molecular weight.

Ethylene oxide. This fumigant is relatively safe, being less toxic than sulphur dioxide. It is self-warning, sublethal concentrations irritating the eyes and nose; in lethal concentrations this irritation is intolerable. The dangerous dose for animals is 3000 ppm for 30–60 min, whereas a concentration of 250 ppm engenders no serious disturbances. Severe exposures of laboratory

animals result in ataxia, dyspnoea, gasping, and death, and the eyes and respiratory organs will be found to be inflamed or afflicted with pneumonia.[219]

Methyl chloride. This compound is used as a propellent in liquefied gas aerosols of HETP or parathion. Its toxicity is such that it dictates the wearing of a respirator, as also do the organic phosphate insecticides.

Carbon tetrachloride. This material, used in household solvents and fire extinguishers, is relatively non-toxic to man and animals, rats and monkeys being able to live indefinitely in an atmosphere of 100 ppm. The lowest concentration detectable by odour is 72 ppm. There are very few fatal human cases in the literature, even although examination of 96 normal men showed that their daily exposures ranged up to 1200 ppm.[197] The maximum concentration tolerable for 1 hr without injury is 5000 ppm.[113]

Continuous exposure of laboratory animals to 400 ppm was found to lead to cirrhosis of the liver, kidney damage, jaundice, and a high icteric index. At half this vapour concentration, the slow damage to these organs is cancelled by regenerative activity.[197] The symptoms involved in exposure to high concentrations are irritation of eyes, nose, and throat, headache, nausea, abdominal pain, diarrhoea, stupor, convulsions, uremia, fever, and death.[113]

Trichloroethylene. The vapour of this dry-cleaning fluid is even less toxic than that of CCl_4,[113] and it has been used as an anaesthetic.[93] Rats and dogs have been exposed to 2000 ppm for 6 months without impairment of their growth, the only effect being a slight drowsiness. A concentration of 3000 ppm caused over 50% mortality, while 4000 ppm of trichloroethylene was completely anaesthetic. Unlike CCl_4, high concentrations did not produce liver or kidney degeneration.[207] The lethal dose for short exposures of laboratory animals is about 30,000 ppm.[113]

The medical profession rates the long-term toxicity of trichloroethylene greater than that of CCl_4, since the literature records 284 cases of poisoning with 26 deaths.[104] It is absorbed through the skin and has been stated to be a nerve poison. The symptoms appearing in man are giddiness, nausea, nervous irritation, stomach disturbances, unconsciousness, and death.

Ethylene dichloride. This widely used fumigant is also less toxic than CCl_4 when inhaled by man, and its odour is noticeable at relatively safe concentrations. No serious disturbances are felt until the atmosphere contains 1000 ppm, and the dangerous level for 30-min exposure is 5000 ppm.[179] Like CCl_4, it may be absorbed through the skin.[117] The initial symptoms are giddiness and nausea, followed by weakness, trembling, stomach cramps, and a drop in blood sugar.[234] Severe exposures of guinea pigs induced irritation of eye and nose, retching, ataxia, and stupor with convulsive movements; the death which supervened was probably mainly due to lesions produced in the lungs.[179]

Methyl bromide. Although CH_3Br is not highly toxic, its odour is not unpleasant and cannot be trusted to give warning of danger. Vapour concentrations of 3000 ppm are dangerous when inhaled for 30–60 min, and 20,000 ppm is quickly lethal. The maximum concentration which can be tolerated by guinea pigs for several hours without serious injury is 50 ppm.[178] Of 90 men exposed industrially to concentrations ranging up to 35 ppm, mild intoxication was shown by 33, and skin lesions by 22.[221]

Methyl bromide is a nerve poison and narcotic, with a characteristic delayed action. Fatal human cases are marked by a long latent period, followed by collapse, convulsions, coma, and death; post-mortem examination reveals profound injury to the central nervous system.[104] Cases reported in the literature are rare. Although many fatalities have occurred in manufacturing and filling plants, and as a consequence of its use as a refrigerant, CH_3Br has a very good record as a fumigant when employed by qualified personnel. It has been found that methyl bromide inhibits the enzyme succinic dehydrogenase, which plays an important part in nerve metabolism, and this effect is considered responsible for the functional disturbances in the brain.[157]

Ethylene dibromide. This more slowly volatile compound is far less toxic than CH_3Br.[104] So far as is known, no hazard is involved in its use as a soil fumigant.[222] However, prolonged exposure of the skin to the chemical should be avoided. When it is encountered in closed spaces, a respirator should be worn. In its use as a grain fumigant, it has been found to be readily adsorbed, but the bread made from the grain shows no unusual

odour or taste and contains less than 2 ppm of the chemical. Ethylene dibromide has been tolerated by rats in daily dosages of 50 mg/kg for 4 months.[2]

Methyl formate. The use of this ester as a fumigant is moderately hazardous, although its irritant properties to eyes and nose make it self-warning. Experiments on guinea pigs showed that 1500 ppm could be tolerated for several hours without serious effects, and that the dangerous level for 30–60 min was 1.5% or 15,000 ppm. The symptoms of lethal concentrations were retching, ataxia, narcosis, and death.[181] Ethyl formate is considered to have a similar moderate level of toxicity to operators.[16] Formate esters and methyl esters are classed as lung poisons or irritants.[113]

Acrylonitrile. This insecticide has such a low vapour pressure that it can be used as a spot fumigant without the necessity of a respirator. However, the maximum safe vapour concentration is only 20 ppm, although this figure is seldom reached with so slight a volatility. The irritant vapour of acrylonitrile is self-warning. Initial symptoms of poisoning in man have been variously described as salivation, eye and nose irritation, skin flush, and rapid respiration;[68] also nausea, asthenia, and occasionally headache and diarrhoea. Anemia and jaundice may appear as chronic symptoms.[231] Lethal doses in animals cause a transient paralysis followed by convulsions before death. Acrylonitrile resembles cyanide in its toxic action, and it is found that the use of sodium nitrite as an antidote increases resistance to the poison.[68]

Trichloroacetonitrile. This compound is of the same moderate order of toxicity as ethylene oxide.[165] Like acrylonitrile, it is self-warning, being highly lachrymatory and irritant to the nose.[46]

Dichloroethyl ether. Since it is not highly volatile, this material may be used in the field without protective measures, although inside fumigation would demand the use of respirators. Its odour is noticeable at 35 ppm and nauseating at 100 ppm, thus giving adequate warning. Guinea pigs have been found to tolerate concentrations of 35 ppm for several hours without manifesting serious disturbances.

The dangerous level for 30- to 60-min exposure is 1000 ppm. Lethal concentrations applied to laboratory animals cause an irritation of eyes and nose, followed by dyspnoea, gasping, and death. It is considered that dichloroethyl ether may be dangerous to man in concentrations low enough to pass undetected but sufficient to cause irritation of the respiratory system.[182]

Paradichlorobenzene. This material may be safely used as a fumigant without precautions, since its volatility is very low. However, it is considered to be no less toxic than benzene,[80] and it is said to cause, like other chlorinated hydrocarbons,[113] damage to the liver. When tested by oral administration, dogs were found to tolerate doses up to 15 gm,[198] and human beings up to 20 gm (equivalent to 300 mg/kg), above which level PDB starts to be harmful.[186] Although the use of PDB in the house is safe, there is a toxic hazard in industrial plants where workers are exposed to the vapour for long periods.

Solvents

Aliphatic oils. The kerosene and gasoline fractions of petroleum oils are readily absorbed through the skin.[147] Inunction of laboratory animals with kerosene results in skin irritation, and in some cases (especially rabbits) in death.[36] The spraying of livestock with petroleum oils reduces the transpiration of water from the skin and impairs their thermoregulatory ability. This is due not only to the physical effect, but also to a physiological poisoning, the unrefined oils of low U.R. content being the more harmful in this regard.[83] A group of calves has been severely injured, and two of their number killed, by application of petroleum-oil sprays on a hot day.[18] A certain proportion of men shows dermatitis on skin contact with kerosene; this sensitivity to kerosene rash disappears on habituation.[31, 94] Observations have been made in India on the hazards of DDT to personnel engaged in its formulation; it was established that any toxic symptoms observed were attributable to the solvent, those of lower boiling point being the most toxic. Gasoline is readily absorbed through the skin, and so is the tetraethyl lead found in anti-knock petrols.[113] Gasoline also presents a vapour hazard, being inflammable and explosive at 1400 ppm. and toxic to breathe at 2000 ppm. The symptoms of poisoning are vertigo,

headache, nausea, and a state of confused excitement. In lethal exposures these are followed by unconsciousness, then convulsions and death from respiratory depression.[93] Kerosene as an insecticide solvent presents a hazard in that it may be drunk by accident; kerosene alone has caused fatalities in children.[17] Oral doses of 2 cc/kg have induced, in the rabbit, tubular degeneration of the kidney and a pronounced parenchymatous change in the liver. However, in checking the role of kerosene in human poisoning by DDT solutions, it was found that baboons were unaffected by oral doses of 22 cc/kg.

Aromatic hydrocarbons. These compounds have been classified as blood poisons. Benzene is a solvent of not inconsiderable hazard; it causes anaemia and leucocytosis, since it attacks the fatty parts of the bone marrow where the erythrocytes are formed. The inhalation of benzene vapour at a concentration of 30 mg/litre may lead to unconsciousness in a few hours, and death may supervene. The incipient symptoms of poisoning are headache, giddiness, weakness, and tremors; the lethal symptoms include delirium and convulsions; and death may be slow in coming. Toluene and xylene are less toxic, since their lower volatility lowers the possible vapour concentrations; the highest safe concentration is 100 ppm. Solvent naphtha, which is a mixture of these compounds together with ethylbenzene, may induce symptoms in cases of prolonged exposure to 5–10 mg/litre and may prove fatal in 15-min exposures to a concentration of 30 mg/litre; the symptoms resemble those caused by benzene, with the addition of epithelial irritation. The saturated naphthene, cyclohexane, is about half as toxic as benzene.[113] Xylene is often used in emulsions for livestock dips. Whereas a concentration of 10% is much too high and causes tremors and convulsions, a level of 2.5% is safe and causes only a slight transitory eye inflammation in goats.[28] Emulsions containing 3.6% xylene have no effect on goats or swine but cause skin desquamation in horses, skin irritation in cattle, and a transient paralysis in sheep.[30]

Naphthalene inhaled as a vapour may cause headache, nausea, visual disturbances, and the appearance of blood in the urine; its ingestion leads to gastric and urinary troubles.[113] The methylnaphthalenes and other alkylnaphthalenes widely used as the *Velsicol* solvents present a slight hazard of dermatitis and of

systemic poisoning from skin absorption and inhalation. Evaluation of this hazard by feeding experiments on dogs reveals that the methylnaphthalenes are no more toxic than kerosene solvents and less toxic than benzene. The main symptoms are loss in weight and slight damage to liver or kidney. When inuncted these solvents have caused irritation and hardening of the skin. Many of the other aromatic oils now in use as solvents for the chlorinated hydrocarbon insecticides introduce similar hazards.[34]

Miscellaneous solvents. Turpentine, containing terpenes, is a pronounced skin irritant. Its vapour is toxic if inhaled for a few hours at concentrations as low as 6 mg/litre. The symptoms include irritation of eye, nose, and throat, headache, and giddiness, and may extend to irritation and damage to the kidney. Cyclohexanone is considered to be a non-toxic solvent and has never produced cases of industrial poisoning.[113] Isophorone, another non-hydrocarbon solvent, is considered to be quite safe for normal use.[34] The vapour of "Freon" (dichlorodifluoromethane), employed indoors in aerosol bombs, is non-toxic even when in 20% concentration in the air.[179a, 239] However, when allowed to evaporate from the hand, it freezes the skin and thus causes third-degree burns.[150]

Arsenicals

The minimum lethal dose of arsenious oxide (As_2O_3) for laboratory animals ranges between 5 and 100 mg/kg [199] (rabbit 20, rat 75, dog 85) when administered orally, solutions being more toxic than powders.[184] The minimum lethal dose for an average man is 130 mg of As_2O_3 [32, 186] (equivalent to 2 mg/kg), or 100 mg of the arsenical ion; that for a hog is 500, a sheep 850, a large cow or horse 2000 mg per individual.[172] Subcutaneous and intravenous toxicities are twice as high; whereas the oral toxicity of sodium arsenite is one-tenth that of As_2O_3, to the rabbit.[111]

The minimum lethal dose of acid lead arsenate ($PbHAsO_4$) for mammals ranges between 100 and 500 mg/kg. It is roughly one-fifth as toxic as As_2O_3 for dog and rabbit [124] (Table 2); for the guinea pig it is half as toxic, the minimum lethal dose being 14 mg/kg.[162]

Although arsenious oxide requires 1–6 weeks to be completely excreted, it is not a cumulative poison unless administered in high chronic doses. Sheep are reported as being able to survive daily doses of 500 mg, and cattle and horses 2000 mg without adverse symptoms,[172] although this is the LD_{50} level (see above). Daily doses of white arsenic are habitually given to mountain horses in the Tyrol to increase their endurance. The human inhabitants of this region may include "arsenic eaters," who seek stimulation by eating As_2O_3 in coarse powder form. Although the toxicity is reduced by the coarseness of the particles, fatalities do occur; but in general it is claimed that the body develops a tolerance for the poison.[186] The controversial question of tolerance for arsenic has recently been demonstrated in the affirmative for As_2O_3 injected intraperitoneally into rats, where sublethally treated individuals eventually were induced to survive dosage levels that were lethal to untreated controls.[158] Chronic doses of 4 mg/kg of lead arsenate to rats daily for 8 weeks were definitely toxic; smaller oral doses were growth-stimulating but caused the degeneration of nerve.[196]

Trivalent arsenic, as in As_2O_3, is a severe gastrointestinal irritant, and the symptoms of acute oral poisoning resemble those of cholera. Within an hour of ingestion by man, the throat feels constricted and severe stomach pains commence, followed by continual vomit, diarrhoea, and micturition, all bloody. The skin becomes cold and pale, respiration and blood pressure are depressed, and severe thirst is felt. Coma and death generally supervene within the day. Emergency treatment involves emetics, stomach lavage, and purgatives; ferric hydroxide is effective as an antidote only if given shortly after the ingestion of the poison.[93] Acute poisoning in livestock involves ulceration and necrosis of the stomach, causing a general depression or even coma; the facial expression, especially in horses, is characteristic.[172] Calves acutely poisoned show progressive paralysis from the hind legs forwards, rapid respiration, and convulsions; they usually die in tetany.[162] Sheep will tolerate sodium arsenite dips containing 0.2% of As_2O_3, in spite of absorbing 60–90 mg of it through the skin and voiding it in saliva and urine.[106] The danger here is that arsenic may be swallowed into the gut, or into the lungs where it may induce bronchopneumonia, or that it may

promote the infection of wounds.[57] Cattle submitted to repeated arsenical dips develop blisters and other injuries of the skin.[126]

Chronic symptoms of arsenical poisoning in man include dark pigmentation of neck, armpits, and eyelids, hardening of palms of hands and soles of feet, puffy edema of face and ankles, and a state of diarrhoea; the victim may come to appear apathetic or idiotic.[93] Records of arsenical poisoning in human beings show skin lesions or keratoses in one-half, gastric symptoms in one-quarter, and nervous systems (tremors, cramps, peripheral neuritis, or epileptic fits) in one-fifth of the cases. Very occasionally, skin cancer has been caused by arsenicals, particularly As_2O_3.[104] In livestock, the only characteristic symptom of chronic arsenical poisoning was found to be a thickening and desquamation of the skin.[172] Calves chronically poisoned showed anorexia, asthenia, and stiffness; they suffered from diarrhoea and became gaunt in appearance.[162]

Arsenic is eliminated by the kidney into the urine, and some may be lost in the faeces and body secretions. When ingested in excess of elimination it accumulates, particularly in the liver, and to a less extent in the kidney, and may be secreted in the milk.[32,172,186] Arsenicals are not very active in causing histopathology, but in high doses they cause fatty degeneration of the liver and the appearance of the red or pale "arsenic kidney." Curiously enough, arsenites are less active in this regard than arsenates, and arsenic causes less kidney damage than lead.[104]

Trivalent arsenic is an inhibitor of the cellular metabolism of organs and tissues, combining with the free SH groups of the dehydrogenase enzymes; arsenate is not, and it is considered that its action first involves its conversion to arsenite.[218] The administration of SH compounds such as cysteine or glutathione has been found to have a protective effect.[217] The most effective protective and therapeutic agent for arsenical poisoning is the dithiol compound 2,3-dimercaptopropanol, termed BAL, which when injected intramuscularly increases the rate of arsenic excretion very greatly.[71] The treatment of chronic arsenical poisoning with sodium thiosulphate to increase urinary elimination has given contradictory results.[93]

The application of arsenicals to field crops involves hazard to the consumer, whether man or domestic animal. Alfalfa which had been contaminated by drift of calcium arsenate dust applied to adjoining tomato fields was sufficiently toxic to kill 75 cows in one California county in a single year; however, the residues involved were as much as 650 ppm of arsenic.[27] The application of 2 lb/acre of calcium arsenate to alfalfa, as in normal practice, involves no hazard since the residues range between 10 and 90 ppm. Winter feeding of cattle, sheep, or horses with alfalfa sprayed at 3 lb/acre caused no symptoms, the normal weight-gain showing reduction only at 6 lb/acre.[82] Even with alfalfa sprayed with 8 lb/acre of calcium arsenate, and carrying residues of 140 ppm of arsenic, the daily intake of a horse or cow eating 30 lb of the forage is considerably less than the 2000 gm (as As_2O_3) it can ingest daily with impunity.[172] Sodium arsenite, applied in Africa for locust control, is much more toxic; cattle die when fed on pasture grass sprayed at 1.5 lb/acre, when they have accumulated a total dose of 4.2 gm (equivalent to 2 gm of arsenic).[111]

Arsenical residues are also a problem in orchards, where the yearly application of lead arsenate has exceeded 100 lb/acre. The hazard to livestock pastured in orchards was tested at the 25-lb/acre level, and it was found that domestic fowl were unaffected, sheep showed symptoms but recovered, but calves died. Even on pasture sprayed at 8.5 lb/acre, the calves lost appetite.[162] Sheep are not killed by lead arsenate until they accumulate a total of 7 gm (= 1.5 gm of As), only 2–5% of it being currently excreted. Lead arsenate deposited upon foliage some weeks before ingestion was found to be considerably less toxic than the fresh suspensions.[203]

Greater hazards are involved in arsenical residues on fruits used for human consumption. The dangerous level, which was set at 0.025 grain/lb of As_2O_3 in 1927 as a consequence of British alarm over American apples, and reduced to 0.01 grain/lb (1.4 ppm) by 1932, was restored to 3.6 ppm in 1940. The arsenical is confined to the skin, since it is not absorbed into the fruit itself. Natural weathering between the last spray and the harvest may reduce the deposit below these tolerance limits. How-

ever, in cases where spraying has been heavy and continued until late in the season, it is necessary to wash off the deposit in dilute HCl before marketing. The olive oil from sprayed olives contains no arsenic; the wine decanted from the mash and sediment of arsenic-contaminated grapes is free of the poison.[74] It should be pointed out that many marine foodstuffs, e.g. fish and lobster, may naturally contain a high content of arsenic.[113] Since retailed tobacco products formerly contained up to 40 ppm of arsenic derived from insecticidal treatments, it was suggested in 1940 that cases of exfoliative dermatitis in heavy smokers, who showed up to 0.24 mg/100 cc of arsenic in their blood, were due to arsenical poisoning from the treated tobacco.[18]

Metallic elements

Lead. In cases of chronic poisoning by small amounts of lead arsenate, the lead is more important than the arsenic.[32] Symptoms of Pb poisoning are more frequent than those of arsenic poisoning, although both may be shown. Whereas most of the injury to the blood is due to arsenic, most of the kidney damage results from lead poisoning.[104] The dangerous level of Pb ingestion is considered to lie between 0.3 and 1.3 mg/kg per day.[32] Men fed 2 mg (0.03 mg/kg) daily for a year showed no symptoms but retained more Pb in the body than those fed 1 mg per day.[120] Since the body accumulates lead at all dietary levels in the soft tissue and bones, the danger is that the stored Pb may become mobilized to stream through the tissues. The tolerance of Pb in the spray residue, which was set at 3.6 ppm, was raised in 1940 to 7.2 ppm (0.1 grain/lb).

The outstanding toxic effect of Pb is hypertrophy of the kidneys; it also makes the bones brittle. External symptoms are loss of appetite, anaemia, and a decrease in growth rate. The amount of lead stored, and its toxicity, may be reduced by a high level of calcium in the diet.[32] The therapeutant BAL fails to protect animals, despite increasing the elimination of Pb, because the Pb-BAL complex is also toxic.[89]

Mercury is highly toxic, and residues of mercurated spray chemicals should be regarded with caution. The practice of fumigating stored grain with mercury vapour leaves no toxic residue on the food.[240]

Antimony, present in tartar emetic used for ant baits and thrips control, resembles arsenic in its toxicity and action on the human system.[113] It accumulates principally in the liver and also in the thyroid and parathyroid tissue. BAL increases its rate of excretion and offers effective protection against poisoning by tartar emetic and other Sb compounds.[72] The minimum lethal dose of tartar emetic for man is 300 mg (5 grains) and for a child 50 mg. It is a gastrointestinal irritant, causing vomiting and purging, sometimes followed by convulsions.[186]

Thallium, also used in ant baits, is a cumulative poison 4 times as toxic as arsenious oxide. It affects the sympathetic nervous system, causes muscular pains, endocrine disturbances, and loss of hair, and leads to rickets.[151a]

Selenium, which may be absorbed into plants to render them immune to phytophagous insects, also resembles arsenic in its action, and its use is therefore restricted to ornamental flowers. It causes abdominal pains, anaemia and loss of weight, cellular destruction of the liver, gradual damage to the kidney, and a general debility.[113] The median lethal dose of Na selenite for the rat is 3–6 mg/kg, for the rabbit 1 mg/kg, and for the cow 11 mg/kg. In Wyoming and other parts of the world where selenium abounds in the soil which supports seleniferous plants, the symptom of poisoning in cattle is the "blind staggers." This is followed by paralysis and death by respiratory failure; with lesions in the main organs, erosion of bone, and ulceration and haemorrhage of the gut. Chronic poisoning, which occurs with rats with 5–15 ppm of Se in the diet, is characterized by emaciation, stiffness, loss of hair, and death from thirst or starvation.[35] BAL does not remove the toxic symptoms, since it forms a toxic complex with selenium.

TABLE 2. Oral Toxicity of Arsenicals and Fluorine Compounds to Mammals [124]

Median lethal doses, mg/kg

	Rabbit	Dog
Arsenious oxide	20	85
Lead arsenate	100	500
Calcium arsenate	50	38
Sodium fluosilicate	138	150
Barium fluoride	200	550

Fluorine compounds

The fluorides, fluosilicates, and fluoaluminates are several times as safe as lead arsenate, and their toxicity is in direct proportion to their fluorine content.[186] The acute oral toxicity of Na or Ba fluoride to the rabbit or dog ranges from 200 to 500 mg/kg[114,124] (Table 2); that of Na fluosilicate to the rabbit or goat ranges from 150 to 200 mg/kg.[14] The lethal dose of Ba fluosilicate was found to be 100 mg for a hen and 170 mg for a pigeon.[118] The chronic toxicity of fluoride is due to its upsetting the calcium balance and precipitating calcium as calcium fluoride. Toxicity is first apparent on laboratory rats at 500 ppm of NaF in the diet, where some mortality results.[58] At a level of 900 ppm of F, whether as fluoride or Na fluosilicate, all animals die in 10 days. The insoluble Ca fluosilicate and Na fluoaluminate (cryolite) require 40–50 thousand ppm to produce a similar death rate.[190] A very low level of fluoride is sufficient to damage the enamel of the teeth; striation occurs in rats at 25 ppm,[58] and mottling in children at 1 ppm in their drinking water. The tolerance for fluorine on apples, established in 1938, is 2.8 ppm (0.02 grain/lb). Where cryolite or Ba fluosilicate sprays are applied, it is usually necessary to wash off the residues. For example, apples sprayed with Ba fluosilicate showed average residues of 5.6 ppm before washing.[186]

The main hazard involved in fluorine compounds is the mistaken ingestion of roach powder. Disasters have occurred in institutions at Salem, Oregon, where 263 cases and 47 deaths resulted from mistaking it for milk powder in making scrambled eggs, and at Pittsburgh, Pennsylvania, where 40 cases and 12 deaths resulted from mistaking it for baking soda in pancakes.[140] The toxic dose for man is probably about 5 gm of Na fluoride. The gastrointestinal mucosa are drastically affected, causing salivation, stomach pain, nausea, vomit, and diarrhoea, the last often bloody. Then epileptiform convulsions set in, followed by collapse with pallor and cyanosis, the blood pressure falls, the pulse may fail, breathing is depressed after an initial stimulation, and death is brought on by respiratory failure or heart failure.[140] First aid involves gastric lavage, and calcium salts provide antidotes to precipitate the fluorine, such as dilute calcium chloride

or milk orally,[93] and intramuscular injection of calcium gluconate.[185] Chronic poisoning by fluorine compounds has been observed industrially, characterized by anorexia, bone fragility, stiffness of the hands, cachexia, and finally respiratory paralysis.[51] However, clothing mothproofed with fluosilicates involves no hazard to the wearer.

Pyrethrins

These esters are rapidly detoxified by hydrolysis in the alimentary canal and tissues of warm-blooded animals,[44] and the chrysanthemum monocarboxylic acid is excreted in the urine.[15] They therefore exhibit no chronic toxicity. The oral toxicity of pyrethrins is so low that they have been used as anthelminthics.[44] A sudden massive oral dose, of not less than 1500 mg/kg for rats and guinea pigs, can cause acute toxicity.[187] Intraperitoneal injection is more dangerous, the LD_{50} for guinea pigs being 100–150 mg/kg, and the LD_{66} for mice being 240 mg/kg of pyrethrin II (pyrethrin I showing lower toxicity).[135] Intravenous injection is highly active, 6–8 mg/kg being toxic to the dog, and no animal can withstand the direct introduction of pyrethrins into its circulation.

The nervous symptoms induced resemble those of veratrin poisoning, proceeding from excitation to convulsions to tetanic paralysis, except that pyrethrins cause muscular fibrillation as well. The clonic convulsions in the mouse have given the animal the appearance of "dancing like a mechanical toy." Death is due to respiratory failure; if, however, recovery occurs, it is complete.[44] The convulsive stages may be prevented by anaesthesia with pentobarbital or ether, and the diarrhoea which occurs may be prevented by atropine.[135]

Pyrethrins offer no residue hazard, particularly since their deposits are labile. They may, however, present certain unexpected hazards to the user, particularly to those who are subject to the "pyrethrum idiosyncrasy." Pyrethrum dusts produce allergic attacks in many persons who are sensitive to ragweed pollen.[76] Cases which resemble anaphylactic shock, and cases of dermatitis, have been recorded in the pyrethrum industry.[48, 118] Loaders of large quantities of pyrethrins have shown vertigo at the end of the day.

The pyrethrin synergists, piperonyl butoxide and *n*-propyl isome, show a low level of acute toxicity, the oral LD_{50} exceeding 10,000 mg/kg in either compound. Although they are not irritant to the skin, multiple inunction of 200-mg/kg doses may be fatal to laboratory animals.[134]

The pyrethrin analogue, allethrin, is no more toxic than pyrethrin concentrates; the acute oral LD_{50} for rats is 920 mg/kg for allethrin as compared with 800–1900 mg/kg for 20% pyrethrins. The LD_{50} of allethrin for mice is 480 mg/kg and as much as 4300 mg/kg for rabbits.[197a] As for chronic toxicity, rats have tolerated 2000 ppm of allethrin in the diet for almost a year, and show no concealed histopathology.[197b] Rats have survived single exposures to aerosols containing 10,000 times the fly-killing concentration, and multiple exposures of 10 times the normal concentration. Its percutaneous toxicity is very low; when impregnated on cloth, allethrin has caused a temporary erythema in rabbits to whose skin it was applied.[197a]

Rotenone

The active principles of *Derris* and *Lonchocarpus* roots are considerably more toxic to fish, insects, and other invertebrates than to mammals. Doses of 50 mg/kg of rotenone will rid livestock of hookworms and roundworms without affecting the host, and man will tolerate oral doses of rotenone as an anthelminthic at 200 mg/kg.[49] Nevertheless, suicide is possible with fresh derris root, and fatalities have occurred from drinking water treated with these fish poisons.[186] Young pigs have been killed, with ataxia and erythema, by drinking the run-off from warble-fly sprays.[160] Toxicological assessments on the basis of the oral dose have shown great variation.[131] Firstly, olive-oil solutions of rotenone are more toxic than fine suspensions and much more toxic than coarse suspensions, the LD_{50} figures for rats being 25, 150, and 1000 mg/kg, respectively.[138] Minimum lethal doses for the guinea pig have varied from 12 to 100 mg/kg, depending on the investigators concerned.[99,138,187] Interspecific variations are great, with m.l.d.'s for guinea pig 60, rat 700, and rabbit 300 mg/kg in one investigation,[99] whereas other workers state that the rat is more susceptible than the guinea pig.[187] There are additional principles in derris root which raise its toxicity above

that of its rotenone content; these include deguelin, tephrosin, and toxicarol, but do not completely account for the rise in toxicity.[138] Acute toxicity figures for derris root taken orally show LD_{70}'s as follows: guinea pig 75, rat 100, dog 150, and rabbit 600 mg/kg.[4]

When injected directly into the blood stream, rotenone is highly toxic. The LD_{50} by intravenous injection of rotenone to mammals and birds lies between 0.3 and 1.0 mg/kg.[99] For intraperitoneal and intramuscular injection it lies between 2 and 10 mg/kg,[187] and for subcutaneous injection between 15 and 20 mg/kg.[99]

Rotenone may exhibit chronic toxicity to laboratory animals. Rats administered 5 mg/kg daily survive for 24 days, and those given 15 mg/kg die within 4 days;[138] those fed 6250 ppm of rotenone in the diet survive for 8 days.[123] Guinea pigs are practically unaffected by doses of 25 mg/kg given 4 times in 10 days.[187] Rabbits show no symptoms when given 30 mg per individual daily, but cumulative poisoning is evident when this dose is doubled (equivalent to 15 mg/kg daily). Young dogs fed 400 ppm of rotenone in the diet remain stunted in their growth.[5]

Rotenone (in derris) is anaesthetic for vertebrate nerve; it exerts its most profound effect on respiration, depressing it after an initial stimulation.[4] It has been considered to operate on the brain, and particularly the medulla oblongata.[37] Its initial administration by any route causes nausea and vomiting in higher animals.[99] Although it is never lethal by inunction,[134] it exerts a numbing effect on the oral mucous membranes of man[4] and is irritating to the mucous membranes and skin of rats.[123] Rotenone dusts can cause severe conjunctivitis in the eyes, and if inhaled sufficiently have proved fatal to a representative selection of laboratory animals. It has been found that the airborne dust in Brazilian timbo mills constitutes a considerable hazard to workers.[133]

Nevertheless, no human fatalities attributable to the use of rotenone as an insecticide have been reported.[134] Probably man is a comparatively resistant species to oral poisoning. Normally residues of rotenone on crops have been eliminated by weathering in the field. However, it should be noted that the absorption of rotenone into the system may be increased by fat in the diet.[187]

Sabadilla

The dust from sabadilla root contains cevadin and other veratrin alkaloids. The veratrin alkaloids are highly toxic, a dose of 0.5 mg/kg administered subcutaneously being lethal to rabbits.[186] They inhibit the oxygen uptake of mammalian muscle and throw it into a state of prolonged contraction; in addition they are marked irritants.[93]

Sabadilla itself is definitely irritating, not only when anointed on the skin, but also when applied as sprays and dusts, to the epidermis and mucous membranes of the rat; it is also a sternutant. However, it has proved to be less toxic than either rotenone or pyrethrins, no deaths being obtainable in laboratory rats.[123]

Ryania

Ryania powder has also proved to be less toxic than rotenone. The acute oral toxicity is represented by the following LD_{50}'s: dog 150, monkey >400, rabbit and mouse 650, rat 1200, and guinea pig 2500 mg/kg. The symptoms were asthenia, tremors, convulsions, and death. Ryania exhibits virtually no cumulative toxicity, since rats, guinea pigs, and chickens survive a diet containing 10,000 ppm for at least 5 months, whereas the same level of rotenone killed all within 3 weeks. Normal residues of 6 ppm of ryania powder on apples were quite harmless to laboratory animals.[125]

Nicotine

Nicotine is extremely poisonous and rapid in action. The minimum lethal dose for man is considered to be 60 mg, and a dose of 4 mg in non-habituated individuals may give alarming symptoms.[93] The lethal oral dose for rabbits is 30 mg/kg, and for most laboratory animals the figure is nearer 10 mg/kg.[134] Intravenous LD_{50}'s are 2–5 mg/kg for cat and dog.[186] Nicotine may readily be absorbed through the skin,[147] 1.2 gm on the epidermis proving rapidly fatal to the cat.[75] Multiple inunctions at the 40 mg/kg level are dangerous.[134] An interesting human case is recorded, where a gobbet of nicotine accidentally dropped on the sleeve caused collapse, despite being wiped off.[186] It may also be absorbed through the tongue and eye more rapidly than

through the stomach, and presumably the vapour may be absorbed by the lung; florists and gardeners working at close quarters are susceptible to these hazards.[75] With orchard spraymen using 0.1% nicotine solutions, symptoms have appeared in certain workers, including a feeling of constriction in the chest, weird dreams, and a violent nausea; the nausea would return with the slightest re-exposure to nicotine. The first warning of contamination was a burning of the skin. All trouble may be avoided by using gas masks (not dust respirators), a skin salve in which nicotine is insoluble, and the maximum clothing coverage, which should be changed frequently.[103]

Nicotine is a nerve poison, whose initial effect is stimulation which quickly becomes depression.[127] Death is due to respiratory failure, resulting not from action on the respiratory centre but from peripheral paralysis of the motor-nerve endings in the respiratory muscles.[92] Initial nervous symptoms in man are headache, giddiness, disturbed vision and hearing, mental confusion, asthenia, and rapid respiration. These are followed by faintness, prostration, difficult breathing, and finally terminal convulsions. If the poison is taken by mouth, the caustic action of nicotine on the digestive tract results in nausea with vomit, and bellyache with diarrhoea.[93] In rabbits, cats, and dogs the stages of excitation, tremors, convulsions, paralysis, and death by respiratory failure are clearly to be seen.[127]

There is no problem of chronic toxicity of spray residues since the nicotine alkaloid is volatile. However, its non-hydrolysable salts do present a residue hazard. Nicotine sulphate in the diet of rats starts to inhibit growth at 60 ppm, mainly because of its reducing the food intake. All rats eventually succumbed at levels of 500 ppm of the sulphate and 1000 ppm of nicotine bentonite or tannate.[232] Although habituation to nicotine increases the tolerance of young rats to sublethal doses, they become no more resistant to lethal doses.

Nicotine is eliminated from the body through the kidneys and the lungs as the unchanged alkaloid.[127] Acute poisoning may be relieved by artificial respiration to tide the subject over the period of respiratory failure. If, however, central medullary paralysis has set in, all attempts at rescue will meet with failure.[93]

From evidence obtained by subcutaneous injection of guinea pigs, nicotine and anabasine are equally toxic.[98]

Dinitro compounds

4,6-Dinitro-*ortho*-cresol is rather more toxic than most organic insecticides, showing an acute oral LD_{50} of 45 mg/kg to rats and 100 mg/kg to goats. For subcutaneous and intraperitoneal injection these figures are 10 and 50 mg/kg, respectively. The LD_{50} of the sodium salt of DNOC is 28 mg/kg for rats, approximately one-third the toxicity of sodium arsenite; the chronic toxicity of this compound is 30 times less than that of sodium arsenite.[3] Goats were found to tolerate a daily dose of 2 gm (equivalent to 50 mg/kg) for 5 days without showing adverse symptoms. Rats showed no ill effects on diets containing 100 ppm of DNOC.[199a]

DNOC raises the body temperature of laboratory animals[3, 61] by some 3–5° C. In human beings it can raise the basal metabolic rate without causing fever, and thus has been used as a cure for obesity, although its toxic level is not far above the slimming dose.[61] It has caused fatalities in men who formulated it without wearing protective clothing or respirators, the latest being two weedicide workers in Norfolk, England, in 1947. The ready absorption of DNOC through the skin, to which it has a fast affinity, makes protective clothing a requisite, as also does the risk of skin sensitivity for certain persons.[110] It is probable that the other dinitro compounds, DNCHP and DNBP, offer similar hazards. Although settling sprays are not toxic to rats if only the noses are exposed, they may prove lethal if the animals are not prevented from licking their hides. DNOC dust may be toxic to man, dyeing the exposed skin deeply and causing a drastic loss of weight. Other sublethal symptoms, from which recovery may occur, include an extremely high basal metabolic rate with a fever of 102° F, rapid respiration and pulse, sweating, coughing, and shortness of breath.[104] Experimental animals fed DNOC have shown necrosis of liver and spleen.

DNOC is occasionally applied for grasshopper and locust control to open range-land where livestock may subsequently wander. There is surprisingly little hazard involved. An area

treated with a 3% DNOC dust applied at 60 lb/acre (= 1.8 lb/acre DNOC) did not affect calves pastured on it for 3 weeks. It has been stated that atmospheric moisture will render DNOC dusts deposits harmless to animals within 2 days of application.[159] A paddock sprayed with an oil solution of DNOC at 10 lb/acre supported goats and sheep pastured on it for 3 months; most of the animals gained weight, although mouth and anus were spectacularly discoloured.

DNBP (4,6-dinitro-2-*sec*-butylphenol) is even more readily absorbed through the skin than DNOC; on the other hand neither DNCHP (4,6-dinitro-2-cyclohexylphenol) nor its dicyclohexylamine salt is absorbed to any appreciable extent. Like DNOC, dietary DNBP induces eye cataracts in ducklings, but DNCHP does not do so. Rats can tolerate 100 ppm of DNBP, and 500 ppm of DNCHP, in their food. The acute oral LD_{50} of DNBP lies between 5 and 60 mg/kg, and that of DNCHP between 30 and 180 mg/kg.[199a]

Thiocyanates

The higher thiocyanates which are used in fly sprays are of a low order of toxicity to mammals. They show the following LD_{50} levels for the laboratory rat: lauryl thiocyanate, 1250 mg/kg; *Thanite*, 1000 mg/kg; *n*-butyl carbitol thiocyanate, 500 mg/kg; *Lethane 60*, 500 mg/kg; and *Lethane 384 Special*, 400 mg/kg. However when administered at fatal levels, they kill within a few minutes.[134] The toxicity of alkyl thiocyanates increases as the series is descended to methyl thiocyanate, which shows an oral LD_{50} of 0.02 cc per rat (60 mg/kg). Subcutaneous injections of thiocyanates are 300–600 times as toxic as oral doses.[160]

All the thiocyanates may be absorbed through the skin in toxic amounts, the lower analogues acting very quickly. A dose of 0.5 cc of *n*-butyl carbitol thiocyanate applied to the skin kills rats within 8 hr. *Lethane 60* and *Thanite* are dangerous when applied to the skin in doses of 500 mg/kg. *Lethane 384* is dangerous when applied in single doses of 500 mg/kg or multiple innunctions of 125 mg/kg. The higher alkyl thiocyanates and *Lethanes* are all irritating to the skin.[123, 134, 160]

The aliphatic thiocyanates are paralytic poisons, but not narcotics, acting on the central nervous system.[205] The lower homologues release HCN in the body, thus giving a cyanide effect; on being inhaled they cause asphyxiation. The higher homologues are relatively stable and cause liver damage; generalized organ damage was observed from *Lethane 384 Special*.[134] Since —SCN is a regular constituent of urine to the amount of 3 mg/day, being a normal detoxification mechanism for the —CN of glucosides occurring in food, it is considered that the body can excrete sublethal doses of thiocyanates.

Miscellaneous organic compounds

Phenothiazine, administered orally to eliminate stomach bots and parasitic helminths, has proved to be practically non-toxic in tests on rats, rabbits, and man.[186] Dogs and cats survived dosages of 15 gm, although sublethal symptoms commenced to be shown at a level of 3 gm per individual. Xanthone, used on apples to destroy codling moth, has proved to be generally safe, although a few cases of skin inflammation have been reported.[167] Azobenzene, used as heat-generated fumigant for greenhouses, is toxic to rats if fed or injected in considerable quantities, but there is nothing to indicate that its vapour is especially dangerous, and a felt-pad respirator is considered a sufficient protection.[25]

HETP and TEPP

Both these organic phosphate preparations are extremely poisonous and rapid in action, and the toxicity of both materials is due to their content of tetraethyl pyrophosphate. The oral LD_{50} of HETP ("hexaethyl tetraphosphate") has been quoted as 7 mg/kg for mammals.[134] Tetraethyl pyrophosphate has been described as 6–8 times as toxic as HETP, and has shown oral LD_{50}'s to rats of 1.4–2.0 mg/kg.[144] Commercial TEPP, which contains 40% tetraethyl pyrophosphate, is 3 times as toxic as commercial HETP, which contains 10–20% of tetraethyl pyrophosphate as its most active compound. On intraperitoneal injection, the LD_{50} for HETP is 4–6 mg/kg, as against 0.7 mg/kg for tetraethyl pyrophosphate.[9]

HETP and TEPP are readily absorbed through the skin, and cause only slight irritation. Lethal dermal applications range between 10 and 50 mg/kg for TEPP, and for repeated inunction the dangerous level for both compounds is 5 mg/kg.[134] Although these phosphates are detoxified in the body, they still may show a measure of cumulative toxicity.[56] There is evidence to suggest that a small drop of pure TEPP in the eye might be sufficient to kill a man.[134] Normally there are few opportunities for chronic oral toxicity, since even in solution TEPP is completely detoxified in a week,[9] and HETP leaves no toxic residue on fruits.

HETP has a strong inhibitory effect on the cholinesterase of mammalian nerve and brain,[56, 67] and TEPP is the most potent organic phosphate known in this regard. This enzyme inhibition is manifested by the rapid appearance of muscarinic and nicotinic effects in the poisoned victim. Dogs and cats show salivation, vomiting, defaecation, urination, and tremors, followed by prostration, opisthotonus, and convulsions;[67] death occurs from respiratory failure as a consequence of increased bronchial secretion and constriction.[56] The first symptoms in man are headache, tightness of the chest, and difficulty in breathing; miosis of the eyes is characteristic, the contraction of the pupils causing a derangement of vision, a very dangerous symptom when experienced by aerial dusters.[222] These sublethal derangements may take a few days to wear off. Permanent injury may be inflicted on the gastrointestinal tract by organic phosphates, HETP causing necrosis of the gall bladder.[134] It also probably exerts a direct effect on heart muscle to induce bradycardia.[29]

For application of HETP, protective clothing and a respirator with MSA canister GMC-1 are recommended.[189] Airing of a greenhouse for 1 hr after the 2-hr application period is a sufficient safety measure. Extensive orchard spraying with 0.01% TEPP in Ohio, where neither special clothing nor respirators were worn, involved only one case of sickness, which was mild and accompanied by a headache which persisted for 2 days.[54] For accidental ingestion, an emetic such as mustard, salt, or soap is advisable.[222] Atropine is useful as an antidote; being an antagonist, it will effectively protect against 3 times the lethal dose of TEPP.[56]

TABLE 3. Toxicity of Certain Organic Insecticides to Higher Animals [134]

Insecticide	Oral Toxicity: Acute LD_{50}, mg/kg *	Oral Toxicity: Chronic m.l.d., ppm †	Inunction Dangerous Level, mg/kg	Pathology
Parathion	3.5	25	50	Enterocolitis
Nicotine	10	60	50	Inanition
Toxaphene	60	Neg.	780	Liver
Rotenone	60	30	....	Liver
Lindane	125	400	50	Kidney, liver
DDT	250	100	2820	Liver, cerebellum
Lethane 60	500	...	5000	......
Chlordane	500	250	1880	Liver
Thanite	1000	600	5000	Liver
Pyrethrins	1500	500	....	None
DDD	2500	2500	2820	Adrenal cortex
Methoxychlor	7000	5000	2820	Kidney

* Average figure for all animals tested; the LD_{50} of rotenone may reach 3000 mg/kg.

† The minimum level hitherto established at which gross symptoms or death occurred.

Parathion

Although parathion (E-605) is considerably less toxic than its oxygen analogue (E-600), it is still extremely dangerous. Determinations of the oral LD_{50} to rats and mice have been variously placed at 3–5 mg/kg [11,134] or 6–10 mg/kg, with 12–24 mg/kg for parathion in the wettable powder form.[10] More recent work has shown, however, that guinea pigs, mice, and male rats show an oral LD_{50} of 25–32 mg/kg, only female rates succumbing at 3 mg/kg.[102] Parathion is hazardous when inhaled, its vapours being extremely toxic,[11] but most aerosol droplets are too large for inhalation. Laboratory animals show complete mortality when exposed to 15% dusts. A lethal dose may be absorbed through the skin, the LD_{50} being 50–65 mg/kg; [10,134] the poison is only slightly or temporarily irritating. Parathion causes transient irritation of the eye; a lethal dose may be absorbed through a rabbit's eye, sufficient to kill the animal in 3 min.

The chronic toxicity of parathion is controversial. It was originally described as being cumulative, doses of 1–2 mg/kg daily[66] or a dietary content of 25 ppm causing symptoms and death in about a week.[134] Later reports aver that parathion is not stored and is rapidly destroyed by the tissues, and that the body cholinesterase can then recover its normal level. Female rats survived a dietary content of 50 ppm to gestate and rear normal young, and male rats were unaffected by a content of 100 ppm of parathion. Dogs showed no abnormal symptoms with daily doses of 1–3 mg/kg.[10] However, lifetime feeding studies in rats indicate that nervous symptoms and cholinesterase reduction begin to appear at dietary levels immediately above 25 ppm.[45a]

Food residues of 3 ppm on kale dusted at 150 lb/acre had no effect on guinea pigs. It is concluded that 2–5 ppm of parathion in a single dietary item would not constitute a health hazard.[134a] Deposits which were 20 ppm initially have decreased to 1 ppm or less at 10 days and 0.1 ppm or less at 30 days after the spray.[5a] Residues on apples treated with parathion as a miticide have seldom exceeded 1 ppm.[222] Residues on citrus fruits quickly weather away from the surface and never reach the interior pulp, but are found in the essential oils of the rind.[37a] Residues on field crops treated at current rates averaged 0.06 ppm at harvest and never exceeded 0.13 ppm; parathion was not translocated to corn within the sheath or to peas within the pod.[91] However, the possibility of the fruit and foliage being poisoned by translocation from the soil (though unlikely) requires investigation. Citrus pickers in California have been driven out by the presence of parathion in a dusty orchard. Workers in Ontario engaged in thinning peaches 2 days after a spray have required hospitalization.

As might be expected, parathion has already claimed its human victims. Three persons have been killed in the manufacturing plant, and the circumstances of death have been quite fully described.[16a] Florists have so far escaped trouble in using parathion aerosols, being unaffected when wearing approved respirators (U. S. Bureau of Mines approvals 2130, 2147, 2149, or 2154; Mine Safety Appliances MSC-1 canister), and encounter-

ing only temporary nausea and headache when omitting to wear one.[170] Spraymen have been less fortunate. A tenant farmer at Raleigh, North Carolina, who sprayed tobacco with 0.1% parathion in wettable powder through the morning and afternoon, with a change of clothing at lunch, collapsed at 4.30 P.M. and died at 9.50 that evening. In this case the concentration he used was excessive, and the machinery was such that he became drenched with spray material. The second case involved a laboratory technician of the University of California, who was applying 0.05% suspension to a citrus orchard with a speed sprayer under favourable weather conditions. At noon he suffered a mild headache, at 4.00 he complained of vertigo, at 4.10 and 4.30 he vomited, and 5.05 he died.[13] The third case involves a labourer in Florida who was engaged in loading speed sprayers with 25% wettable powder. He had previously been incapacitated by the parathion and had been warned to be more careful. But he would not wear a respirator, and was rash enough to stir the powder with his bare hands; he was killed by skin contact and inhalation of the poison.[126a]

There is a case of mortality which indicates the lethal dose of parathion for humans to be no more than 2 mg/kg. It concerns Professor Velbinger, who ingested 120 mg of E-605 and was paralysed so quickly that he could not take any of the prepared antidotes at hand before he died.

Parathion is an anticholinesterase and elicits the characteristic muscarinic symptoms.[66] They include lachrymation, salivation, intestinal hypermotility, and generalized fibrillary tremors; death results in 1 day, usually from respiratory failure.[102] Early symptoms of parathion poisoning in man are characterized by anorexia, nausea, giddiness, headache, and excessive sweating and salivation; later symptoms are diarrhoea, pallor, blurred vision, a tightness of the chest, and twitching of the head muscles.[37a] The symptoms are slower in onset than with HETP or TEPP, and there is no direct slowing of the heart. Parathion causes miosis of the eye; this symptom is reversible. Tissue damage caused by this poison includes enterocolitis in the alimentary canal and necrosis of the gall bladder.[134] Antagonists of parathion include atropine, eserine (physostigmine), nicotine, and $MgSO_4$, of which the first two are best for protection.

increasing the dose required to kill by 6–8 times.[66,102] The antidote recommended in cases of parathion poisoning in operators is 2 mg of atropine, followed if necessary by hourly doses of 1–2 mg up to a total of 10–20 mg/day; this should be given by a physician, for atropine itself is dangerous to be carried by the operator. Protective clothing * should include a plastic raincoat and rainhat, as well as natural rubber gloves, not synthetic rubber, leather, or cloth; a respirator should be donned, with chemical cartridge respirator MSA CR-45779, Willson 701, or American Optical R-5055.

Systemic insecticides

The translocatable and insecticidal compound OMPA, bis(bisdimethylaminophosphonous) anhydride, is much less toxic than parathion. The oral LD_{50} figures were found to be between 10 mg/kg[67a] and 22 mg/kg for rats, 35 mg/kg for guinea pigs, and 60 mg/kg for rabbits. Its median lethal dose on skin inunction was 200 mg/kg, as compared with 63 mg/kg for parathion.[175] Although it is itself not an anticholinesterase, it is converted by plant tissue, or by the liver of the consumer, into an anticholinesterase. Its toxic action is apparently cumulative.[67a] It is established that crops treated with this systemic insecticide may be safely eaten 2 months after the application of the spray.[175]

The systemic insecticide bis(dimethylamino) fluorophosphine oxide is much more toxic, the oral LD_{50} for mice being 2–5 mg/kg. It is therefore too poisonous for use on plants grown as food.[146]

The new acaricide EPN appears to be only one-fifth as toxic as parathion, from investigations of its chronic toxicity to mammals. The dimethyl analogue of parathion shows one-tenth of the dermal toxicity of parathion, but its oral toxicity is still high.[134a]

DMC and DCPM

These chlorinated acaricides do not present a serious toxicity hazard. DMC is less toxic than DDT on the basis of the acute dose, the oral LD_{50} for white rats being 500 mg/kg. As far as chronic poisoning is concerned, it is far less toxic than DDT,

* Fabric clothing may absorb sufficient parathion to incapacitate the laundress (Ontario, 1950).

since rats can survive a dietary content of 1000 ppm without showing any symptoms or significant weight differences from the controls. DCPM has proved to be approximately one-tenth as toxic as DDT on the basis of both acute and chronic oral toxicity. It is not absorbed through the skin in appreciable quantities, nor is it definitely irritating to the skin. The new mite ovicide K-6451 (*p*-chlorophenyl *p*-chlorobenzenesulfonate) is less than one-eighth as toxic as DDT. The acute oral LD_{50} for rats is 2000 mg/kg, and the chronic toxicity is such that 300 ppm in the diet may be tolerated without symptoms. Liver damage appears at dietary levels above 1000 ppm, and kidney damage above 3000 ppm.

Toxaphene

Chlorinated camphene shows a moderately high level of acute toxicity, being about 4 times as toxic as DDT. The oral LD_{50} for rats is 60 mg/kg,[134] and for sheep and goats approximately 200 mg/kg. Dogs and cats are more susceptible,[151] a single dose of 20 mg/kg causing convulsions and 60 mg/kg killing within 3 hr. Administration in peanut-oil emulsion gives lower LD_{50} figures for toxaphene than corn-oil solutions.

Toxaphene is quite readily absorbed through the skin, the dangerous levels being 800 mg/kg for single and 40 mg/kg for repeated inunctions.[134] In this respect, rabbits and guinea pigs are more susceptible than dogs. Toxaphene dusts involve no skin hazard, and multiple exposure to toxaphene sprays has elicited no toxic manifestations in human beings. Whereas this material is classed as moderately irritating to the skin, patch tests have produced no evidence of skin sensitization in man. The 0.5% emulsion dips and sprays now employed have shown no injury to cattle or their calves. But two applications of 1.5% emulsions cause symptoms of poisoning in calves, and 8% emulsions kill them; 8% suspensions, however, allow complete recovery.[151a] Except in rare instances, cattle can withstand treatment with 4% emulsions, whereas the majority of sheep are adversely affected at this level. Emulsions containing 1.5% toxaphene were found to be safe for cattle, sheep, horses, and goats.[36]

Chlorinated camphene first acts by stimulating the central nervous system, thus leading to generalized convulsions and finally death by respiratory failure. In calves, histopathology has been observed in the lungs, which turn a brilliant purple in color. Sodium pentobarbital has been found to give almost complete protection against moderate lethal doses.[12,164]

Although it shows the highest acute toxicity of the chlorinated hydrocarbons, toxaphene has the lowest level of chronic toxicity. As much as 1200 ppm is tolerated in the diet without any symptoms appearing. Steers and lambs may be pastured on alfalfa sprayed with as much as 8 lb/acre of toxaphene and show only temporary nervous symptoms.[145] It is presumed that the liver detoxifies chlorinated camphene as readily as it handles camphor.[134] However, ingested toxaphene may accumulate in the fatty tissues. Cattle and sheep fed for 4 months on alfalfa sprayed twice with 2 lb/acre showed 300 ppm of toxaphene in the fat and 7 ppm in the lean meat; when the applications were 1 lb/acre these figures were 25 and 1 ppm, respectively.[60]

Chlordane

The acute oral toxicity of technical chlordane is no greater than that of DDT. Median lethal doses of this mixture of chlorinated hexahydroindenes have been variously reported for rats at 250, 500, and 750 mg/kg.[112,134,151] For goats the oral LD_{50} was 180 mg/kg, and for sheep between 500 and 1000 mg/kg. Whereas doses of 50 mg/kg had no effect on cattle, a dose of 80 mg/kg gave rise to quite severe and lasting symptoms in sheep.[226] Dogs showed varying responses, some being thrown into spasms at 200 mg/kg, whereas others were unaffected by 700-mg/kg doses.[19]

Technical chlordane is toxic by inunction, with a dangerous level of approximately 2000 mg/kg, and is moderately irritating to the skin. The undiluted material may in a few cases produce dermatoses. Repeated applications of chlordane are dangerous at a level as low as 40 mg/kg.[134] It is found that 4 successive sprays or 6–8 dips of 1.5 or 2% emulsions or suspensions of chlordane are sufficient to kill goats, sheep, and cattle. Once symptoms of poisoning have started to show, the animal is doomed; cattle and goats die within 2 days, sheep within 2

weeks.[171] A single spraying with these materials is sufficient to kill a high proportion of the calves. Pigs and horses escape this hazard entirely.[30]

The chronic toxicity of technical chlordane is no less than that of DDT, and the general toxicity hazard is at least 4 times that of DDT.[134a] Diets containing 250 ppm induce gross symptoms, and a content of 600 ppm proves lethal to dogs within 4 weeks.[134] Although rats survived daily doses of 10 mg/kg, they succumbed to weekly doses of 75 mg/kg in 4 months.[112] It is concluded that chlordane should not be used where there is any chance of food contamination.[134a]

The initial symptoms of chlordane poisoning are similar to those of DDT,[112] being manifested by rats as anorexia, hyperexcitability, and tremors. Symptoms in large livestock are more violent: they include ataxia, blindness, bleating, or groaning, convulsions with opisthotonus and a paddling action of the limbs, and cyanosis before a death in agony; the incidence of blindness is peculiar to chlordane and is not found with DDT.[171] The histopathological changes observed in rats include edema, congestion and haemorrhage of the lungs, and pitting of the kidneys;[112] liver necrosis is also reported.[134] In livestock, large and small (petechial) haemorrhages were found in the intestines, in the heart, and often in other parts of the body; the brain and spinal cord were congested, and the liver was swollen and fatty. These lesions resemble those caused by chloroform or other organic chlorides.[171] It is therefore considered that chlordane destroys, by chloride poisoning, a liver that could normally detoxify it if the doses were moderate.[151] Thus a sheep which was given a dose of 80 mg/kg and allowed 10 days for the symptoms to subside became completely susceptible to daily doses as low as 20 mg/kg and died within a week, liver necrosis showing on post-mortem examination.[226]

The appreciable volatility of chlordane reduces the hazard of toxic residues on crops by ensuring that they are reduced to negligible proportions within 2 weeks. The residues from a 1-lb/acre spraying on alfalfa fell from 18 to 3 ppm in 15 days; and from a 2.5-lb/acre spraying on clover, from 24 down to 2 ppm in 30 days. When treated with 1 lb/acre of chlordane, clover could be fed to ewes and lambs, and alfalfa to rats and

yearling heifers, without any untoward effects.[88] Pasture sprayed at 4 lb/acre had no effect upon sheep confined to it for 3 weeks.[226]

Heptachlor is about twice as toxic to higher animals as technical chlordane, of which it is an active constituent. The dangerous levels for its inunction, whether in single or multiple doses, are one-half those for chlordane.[134]

Aldrin has shown quite high acute toxicity to albino rats, the LD_{50} being 40–50 mg/kg. It is reported to have a high level of chronic toxicity, involving liver damage. However, rats have remained apparently normal for 6 months on a diet containing 75 ppm of aldrin. Moreover, calves have been successfully overwintered on hay sprayed at 1 lb/acre, and dairy cattle have given aldrin-free milk from hay sprayed at 0.5 lb/acre.

Dieldrin is slightly less toxic, the acute LD_{50} values for rats being 50–75 mg/kg, and for sheep and pigs approximately 50 mg/kg. The symptoms of poisoning with dieldrin may be delayed for several days.[134a] The chronic effect of dieldrin in the diet of rats is marked by anorexia, loss of weight, and finally convulsions. Both aldrin and dieldrin are quite poisonous when applied to the skin, and they give no warning in the form of irritation. Nevertheless, emulsion sprays of dieldrin have proved harmless to calves at levels (0.1%) at which lindane was lethal; pigs could withstand 4% dieldrin sprays; and rats have survived daily inunctions totalling 2000–3500 mg/kg of dieldrin.[171b]

Benzene hexachloride

BHC prepared by the usual method, and containing 12–13% of the gamma isomer, shows an oral acute LD_{50} to laboratory rats of 1250 mg/kg,[188, 208] and to white mice of 700 mg/kg.[85] Two early preparations showed oral LD_{50}'s ranging between 1000 and 15,000 mg/kg to mice, rats, rabbits, guinea pigs, cats, sheep, chicks, and pigeons, from which it was concluded that BHC is significantly less toxic than DDT.[97] Sheep could recover from doses of 2000 mg/kg, after 6 days of sickness.[226] Cows and steers were entirely unaffected by doses of 75 and 125 mg/kg, respectively;[88, 226] but calves were severely affected by oral administration of 300 mg/kg.[233] Dogs were scarcely affected by doses of 400 mg/kg of a preparation containing 35% of the

gamma isomer. The greater part, but not all, of the mammalian toxicity of BHC is due to its content of this isomer.[85] The acute oral LD_{50} of the gamma isomer is 190 mg/kg for rats, with an average level of 125 mg/kg for mammals generally. That for the delta isomer is 1000 mg/kg, and for the alpha isomer 500–1700 mg/kg, while the beta isomer is non-toxic at 6000 mg/kg.[134, 188] The gamma isomer is not irritant, but the other three isomers are strongly irritant to the eye, nose, throat, and skin.[176]

BHC is sufficiently non-toxic by the skin-absorption route to enable rats to withstand daily inunction of tails and ears with 5% emulsion for a fortnight without showing symptoms.[188, 225] Mice can be dipped once in 5% emulsions with impunity provided they are not allowed to lick their hide; however, 10% emulsions are lethal. Cattle can survive a single dip in 5% BHC suspension without showing symptoms; and sheep, goats, hogs, horses, and cattle are similarly unaffected by eight dips in 1.5% suspensions within a month.[30] Lindane, the gamma isomer, is, however, dangerous when inuncted once at the 50-mg/kg level or repeatedly at the 20-mg/kg level; it is also irritating to the skin.[134] Thus it is found that a single spray of 1.5% lindane suspension will kill all cattle, only the 0.25% dilution proving entirely innocuous. Calves are all killed when sprayed with 0.05% lindane emulsion, whereas the suspension affects only a minority of them.[30]

The chronic toxicity of BHC is much less than that of DDT. Rats were found to maintain their normal growth rate and health despite receiving daily doses of 500 mg/kg for 57 days.[208] Sheep to which 50-mg/kg doses were administered daily showed slight nervousness and intermittent ataxia, and some of them failed to gain weight.[226] Cattle could tolerate weekly doses of 125 mg/kg of BHC, which were sufficient to protect them from the attentions of the tsetse-fly and the east coast fever tick.[233] Mice could survive daily doses equivalent to 40 mg/kg of BHC for 30 days.[8] With the gamma isomer, rats were unaffected by diets containing 30 mg/kg daily,[208] but the dangerous level for mammals is considered to be 400 ppm of lindane in the diet.[134] The dietary levels at which the BHC isomers begin to retard the growth of rats were 100 ppm for the beta, 800 ppm for the alpha, and 1600

ppm for the gamma isomer; technical BHC did not give growth retardation until 800 ppm was reached.[78a]

Lindane is metabolized quite rapidly and does not accumulate to any great extent in body fat.[134a] It appears in the body tissues in concentrations about equal to that in the diet, mainly in adipose tissue and the kidney; unlike DDT, lindane is taken up in the brain.[129] When BHC is applied to livestock for fly, louse, and tick control, it is not laid down to the extent of tainting the meat.[52] BHC is secreted in cow's milk; when a cow was administered a 40-mg/kg dose, her milk contained about 5 ppm of lindane and smelled characteristically musty for about 10 days after.[86] The alpha isomer shows similar chronic toxicity to lindane (400 ppm being the dangerous level); it gives rise to some trichlorobenzene and possibly trichlorophenol in the urine.[236] The delta isomer, absent in commercial BHC preparations, is one-eighth as toxic (3200 ppm being the dangerous level). The beta isomer shows a comparatively high chronic toxicity—a level of 10 ppm producing gross effects—which is sharply contrasted to its lack of acute toxicity.[134] The tentative limit placed upon stored foodstuffs in the United Kingdom is 2.5 ppm of lindane or approximately 20 ppm of BHC (tolerance set in 1950).[87]

The principal pharmacological action of lindane on the mammal is to stimulate the central nervous system. This results in a rise in blood pressure, a fall in the rate of heartbeat (bradycardia), and the *grand mal* type of encephalogram. The beta and delta isomers of benzene hexachloride are nervous system depressants and may partially eliminate, by antagonism, the effects of lindane.[149] The symptoms of BHC poisoning in laboratory animals are typical of nervous derangement: excitation, tremors, ataxia, convulsions, paralysis, and death in agony from respiratory failure. In sheep, ataxia, tremors, spasms, temporary blindness, and an intense sialorrhoea have been recorded;[97, 226] in cattle, hypersensitivity and tremors precede a general paralysis.[233] In calves, two syndromes have been detected which may be concurrent: stimulation, which involves salivation, grinding of the teeth, rolling of the eyes, excitation, twitches, and convulsions; and depression, involving dullness, failure to eat or drink, and apparent blindness; the final state is one of opisthotonus with the limbs paddling, and death in agony.[30]

The histological changes wrought by BHC and lindane include enlargement of the liver,[78a] necrosis, congestion and fatty degeneration of the liver and kidney, congestion of the bladder with desquamation of its epithelium,[233] haemorrhages in the gastrointestinal tract,[85] heart, and lungs, and edema of the brain and spinal cord.[30] Most of these symptoms may be attributable to organic chloride, since they are also induced by chlordane and toxaphene. Liver damage has been noted for the beta isomer, and liver and kidney damage for the alpha isomer, but no damage has been reported for the delta isomer.[134]

The barbiturates show promise as antidotes to BHC, since pentobarbital or phenobarbital was found to protect cats and dogs from acute poisoning. Atropine prevents the bradycardia, but pentobarbital is required to counteract the rise in blood pressure. Contrary to a theory that the one masquerades as the other, *i*-inositol was found to have little protective action against lindane poisoning.[149]

DDT

The acute oral toxicity of DDT to mammals is indicated by a general LD_{50} figure of 250 mg/kg,[134] which has been established for laboratory rats.[112] This species is more susceptible than other mammals, which may be arranged as follows in order of increasing susceptibility: pig, guinea pig, sheep, goat, cow, rabbit, mouse, and rat.[122] It is considered that man is one of the more susceptible species. Toxicity figures for five species of laboratory animals are shown in Table 4. The effect is greatly enhanced when DDT is dissolved in dietary fat, in contrast to bulk crystals in a fat-free meal.

TABLE 4. Acute Oral Toxicity of DDT
LD_{50}'s, mg/kg

Species	Suspension in Aqueous Gum Arabic[227]	Solution in Corn[237] or Olive Oil[192]
Rat	500	150
Mouse	1600	450
Rabbit	275	300
Guinea pig	2000	560
Cat	1000–2000	250

Goats survive doses of 1000 mg/kg but are killed by a single dose of 5000 mg/kg, dying after 5 days.[211] Sheep can survive doses of 2000 mg/kg after showing tremors, ataxia, and slight paralysis.[163, 226] For cattle, the LD_{50} denoting acute oral toxicity has been taken as 440 mg/kg.[227a] Chickens are unaffected by a dose of 500 mg/kg but are considered to be more susceptible than cattle.[122] The acute LD_{50}'s for subcutaneous injection are no lower than for oral ingestion, ranging from 250 to 1000 mg/kg.[36, 211] The figures for intravenous injection are much lower, ranging from 25 to 75 mg/kg, for dog, monkey, rat, rabbit, and cat in order of increasing susceptibility.[166]

DDT may be dangerous by reason of its absorption through the skin, when applied in solution in oil or other organic solvents. Inunction of ether or kerosene solutions of DDT reveals an LD_{50} of 3000 mg/kg for the rat, 1000 mg/kg for the guinea pig, and as low as 300 mg/kg for the rabbit.[36] The generalization has been made that 4 times the oral dose is necessary for the same effect by inunction.[227a] Whereas DDT solutions may be toxic to the skin, suspensions and powders are not; DDT-impregnated clothing may be worn continuously without hazard. A dose of 4000 mg/kg, which is toxic to the rabbit when dissolved in organic solvents, is not toxic at all if applied as an aqueous suspension or powder, even when application is repeated every day.[36, 63] Daily powderings with DDT crystals or formulated dusts were found to be completely harmless to laboratory animals. A cut wound offers no special entrance for DDT to cause symptoms.[63] The eye is not affected by DDT applied in ointments or emulsions, and is not a point of entry for general poisoning.[227]

DDT is not irritating to the skin.[131] Whereas technical-grade material encounters skin sensitivity in guinea pigs, purified DDT has no effect. Dissolved DDT inuncted on the human inner forearm has been found to abolish the tactile sensation there, the solvent enhancing this effect.[45] Laboratory animals can withstand daily inunctions of 10 mg/kg of DDT in solution. Rabbits are killed by 3 weeks of daily inunctions of 50 mg/kg in kerosene; rats and guinea pigs survive 100 mg/kg daily for this length of time.[64] All three species are killed by daily inunctions of 150

mg/kg in dimethyl phthalate for 1 week. Dogs, however, can survive daily inunctions of 1200 mg/kg of DDT.[63]

Cattle, sheep, goats, pigs, and horses are entirely unaffected by a single application of 8% DDT emulsion.[30] This is a level at which the other chlorinated hydrocarbons—chlordane, toxaphene, and lindane—all induce symptoms and even death.[171a] Skin application always introduces the hazard of oral ingestion, particularly in animals that habitually lick themselves, such as cats where louse or flea powders are concerned, and cattle in the case of livestock dips.[116] The factor of licking was found to be much more important than abrasion, desquamation, or weathering in removing DDT deposited on cattle by 2% suspension dips.[101] But cows could withstand the application of a concentrated emulsion containing 10 gm of DDT 11 times a week for 12 weeks, and showed no symptoms, no change in weight, and no reduction of milk yield, and gave birth to normal young.[212] Cattle inuncted with 22.5 gm of DDT every week for 15 months remained in good health, although gaining slightly less weight than untreated control animals.[8]

Aerosols and mists containing DDT, such as are put up in buildings for the control of household and livestock insects, are of negligible toxicity. For most experimental animals, toxicity does not appear until a concentration of 20 mg/litre of DDT is reached, which is about 4000 times the concentration of 0.005 mg/litre required for insect control.[154] It is considered that inhalation of some of the finer aerosol droplets is possible, and that absorption of DDT may occur in the lungs.[35,153] The most dangerous droplets are those below 5 μ, which are the least effective for insect control. With dusts, maximum retention occurs in the lung alveoli when the average diameter is 1 μ. Mice are comparatively susceptible to DDT mists, succumbing to concentrations of 12 mg/litre, presumably owing to skin absorption and oral ingestion. They are also susceptible to a similar concentration of DDT dust, due to ingestion by licking.[174] To most animals except mice, the inhalation of DDT dust is a minor hazard.[117] The smallest animals, and the youngest specimens of them, are the most susceptible to DDT dusts and aerosols.

The acute symptoms of DDT poisoning characteristically involve the neuromotor apparatus. As observed in laboratory animals, particularly the rat and dog, they start with a period of nervousness and hyperexcitability, with excessive blinking, cold skin, ruffled fur, lack of appetite, and muscular weakness, followed by the onset of fine tremors, due to muscle fibrillation, particularly in the heart muscle, the hind legs, and back.[35, 36, 214, 227] In cases of chronic poisoning by a low concentration in the diet, there is no anorexia and the food intake is normal;[78] the basal metabolic rate rises, probably as a consequence of an increased muscular respiration,[115, 174] and the liver glycogen is depleted.[131] The tremors appear more readily in younger, faster-growing animals, in females rather than males, and in starved rather than fully fed individuals.[78] The continual shaking of the body muscles, coupled with the anorexia, causes a rapid loss in weight.[35] There may be anaemia and leucocytosis of the blood.[36, 64] Advanced poisoning leads to paralysis and clonic convulsions,[117, 167] and death occurs as soon as they cease.[214] Symptoms recorded in sheep and cattle include nervousness, an excited and wild stare, tremors, ataxia, diarrhoea, anorexia and weight loss, slight paralysis or lameness, and convulsions.[116, 163, 226]

The outstanding histopathological effect of DDT poisoning is a necrosis of the liver, similar to that caused by chloroform, CCl_4, PDB, or any of the chlorinated hydrocarbon insecticides.[117] The necrosis may be preceded or accompanied by vacuolization, coagulation, fatty degeneration,[139] hypertrophy,[130] and a slight tendency to tumours.[78] The liver may increase up to 40% in weight, with a high percentage of fat; these fatty livers cannot be corrected by choline treatment.[177] The damage is regenerative in its early stages;[36] but if further chronic doses prevent its regeneration, the detoxification mechanism of the liver for DDT is impaired.[35] One consequence is the accumulation of serum bilirubin and the appearance (in human beings) of jaundice.[23]

DDT poisoning may involve a slight necrosis of the kidney. Histopathology of this organ includes hypertrophy in rats,[130] congestion and friability in horses,[163] and slight tubular degeneration in rabbits chronically poisoned.[193] However, DDT has no effect on renal function.[23] Some muscles, particularly those of the hind leg, may show necrosis.[64, 78, 116] DDT-poisoned rabbits

have exhibited a necrosis of the stomach mucosa and gall bladder.[64] Haemorrhages of the heart, stomach, and intestine have been found in the larger livestock.[117,163] Thyroid degeneration, testicular atrophy, and fibrosis of the ovary have been observed occasionally in laboratory animals.[64,78]

The neurotoxic effects induced by chronic DDT poisoning in dogs resemble those caused by removal of the cerebellum.[23] It is considered that the disturbances of the central nervous system caused by DDT probably extend to the motor cortex and cerebellum,[35] and that the cerebellum is likely to be the critical site of action.[50,134] Vacuolization, tigrolysis, and pyknosis of the ganglion cells have been observed in the brains of cats and rats killed by chronic poisoning.[139,167] However, no lesions of the central nervous system have been observed in larger animals.[117]

Antidotes for DDT poisoning include barbiturates and other nerve sedatives. Phenobarbital, dilantin, or pentothal sodium has been recommended, or the administration of magnesium sulphate by stomach tube. Emergency measures that may be taken in cases of accidental DDT ingestion include saline purgatives, emetics, and stomach lavage.[35,116,117] Fats should be withheld from the diet. Calcium gluconate, which relieves the hypocalcaemia accompanying nervous disturbances, has been found to relieve the toxic symptoms in dogs.[215] Urethane has saved the lives of DDT-poisoned rats,[192] but it is unsatisfactory for human use.

Normally, when DDT is ingested, between 50 and 95% of it is absorbed.[117] Absorption may be less than 50% if undissolved DDT is taken in large amounts. Solution in oil aids absorption.[238] However, when administered in low chronic doses, the insecticide is absorbed as readily in solid form as in solution.[78] Acutely poisoned rabbits show DDT in all tissues and body fluids, and in the faeces but not in the urine.[128] Animals that have received sublethal doses for some time will be found to have accumulated DDT particularly in the body fat and bile;[117,238] the greatest concentration occurs in the perirenal fat.[130,141] Sheep whose diet had contained 100 ppm of DDT showed up to 145 ppm in the body fat, as against only 1 ppm in the muscle.[230] Young pigs, fed 550 ppm in their diet until they attained motherhood, collected 300 ppm in the body fat, 2–4

ppm in the liver, and 1–32 ppm in the kidneys.[59] Dogs fed 50 mg/kg daily for 2 years accumulated the astonishing concentration of 4940 ppm (= 0.5%) in the fat. This could be almost entirely eliminated in 80 days, DDT being detectable in the urine for the first 3 weeks.[238]

DDT is only slightly susceptible to metabolism and excretion by the body; it therefore accumulates in the body fat. It is destroyed to some extent by the liver[236] and is excreted as the breakdown product DDA (dichlorodiphenylacetic acid),[228] either as the free acid or as hydrolysable esters.[236] DDA itself is slightly toxic, the oral LD_{50} to the rat being 2000 mg/kg, and death occurring in 24 hr, accompanied by dyspnoea and asthenia; it is more toxic to the mouse[62] but virtually non-toxic to the cat.[174] A sublethal dose of DDT is excreted by man for a period of 2 weeks after its ingestion, with a peak on the third day;[155] only 20% of the insecticide has been converted to DDA.[191] Rabbits exhibit much the same urinary composition, but cats excrete very little DDT in the urine and apparently store most of it in the body.[193]

DDT is therefore a cumulative poison. Feeding experiments have revealed that rabbits may be killed in 3 weeks by daily doses of 50 mg/kg;[36] the single lethal oral dose is 300 mg/kg.[192] However, rabbits are unusually susceptible in this regard;[117] for monkeys will survive daily doses of 50 mg/kg for a period of 16 months without showing any effects at all.[33] With guinea pigs, no symptoms appear until the daily intake is 40 mg/kg (given by 1000 ppm in the food); with rats and mice, symptoms appear at the 500-ppm level.[237] But long-term experiments with rats, running for 2 years, have shown that nervous tremors eventually appear at the 400-ppm level, accompanied by retardation of growth and an increase in the normal mortality rate of the females, but not the males.[78] At the 1000-ppm level, equivalent to a daily intake of 60 mg/kg, there were still survivors at the end of a year.[237] At dietary levels below 400 ppm there was no increase over the normal mortality rate;[237] but even at 100 ppm the rats were abnormally irritable,[78] and at the end of the 2-year period post-mortem examination revealed liver damage.[33] Therefore the lowest level of dietary DDT giving gross effects may be considered to be 100 ppm.[134] As far as more subtle effects are

concerned, rats fed continuously on 50 ppm of DDT produce offspring which are smaller at weaning and show a lower survival rate. Even when the dietary content is only 5 ppm, the rats eventually develop a detectable amount of liver damage, consisting of cell enlargement and cytoplasmic changes.[69,130a] However, it must be observed that removal of DDT from the diet for 2 months is sufficient to allow complete recovery from this order of liver damage.[78] With the dog, the neurological symptoms that started with daily doses of 100 mg/kg were reversible up to a level of 250 mg/kg, beyond which evidently irreversible damage had occurred to the central nervous system.[23]

Acute poisoning of livestock by DDT is unlikely to occur, but chronic poisoning is possible.[116] Sheep fed daily doses of 100 mg/kg in the diet developed nervous symptoms within 10 days but survived for at least 2 months.[226] In a 3-week experiment where the 100-mg/kg level was raised to 200 mg/kg early in the experiment, cows exhibited severe nervous symptoms, horses showed only a loss of weight due to the resultant anorexia, and sheep were apparently unaffected; however, all the animals developed haemorrhages in the heart and gastrointestinal tract.[165] It has been suggested that the "X disease" of cattle, which appeared in various parts of the United States about 1947, and whose symptoms are anorexia, watery discharge of eyes and nose, skin thickening, and loss of condition, bears a remarkable resemblance to DDT poisoning.[24] Of a number of goats fed 250 mg/kg daily, the majority developed anorexia and tremors within 3 weeks.[211] Pigs fed 7 mg/kg daily were entirely normal and gained weight,[227a] and young pigs could attain motherhood on a steady diet of food containing 550 ppm without showing any symptoms of poisoning, although they accumulated up to 300 ppm of DDT in their fat. Cows fed silage containing DDT so that their daily intake was 9 gm per individual, i.e. 18 mg/kg, showed no toxic symptoms. Cattle fed 50 mg/kg daily for 5 months showed no effects. Steers fed on silage from a crop containing 3 lb/acre of DDT grew perfectly normally.[58] Cows grazed on pasture sprayed at 2 lb/acre revealed no symptoms, but at 7.5 lb/acre they showed stiffness of the joints. Goats and sheep remained entirely normal on pasture treated at 7.5 lb/acre.[200] There is an early reference to ewes, grazed on land

treated at 4 lb/acre, developing extreme symptoms of poisoning; but these were reversible on removal of the animals to fresh pasture.[47]

DDT is secreted in the milk of mammals, having accumulated in the butterfat formed in the body. Since very young animals are more susceptible to DDT poisoning than at any later stage, the sucklings of rats may be killed by their own mother's milk. Goats fed a high level of DDT (250 mg/kg daily) were found to secrete enough DDT in the milk to kill rats and kittens, and to kill suckling rats by being fed to their mothers; the goats' milk flow ceased after 2–3 weeks.[210] If the DDT was given in a single dose of 1500 mg/kg, the milk remained toxic to rats for 1 week.[209] If the chronic dose was reduced to 20 mg/kg daily, the milk was no longer toxic to rats nor did it induce nervous symptoms. Skin application of DDT could not make the milk of the goat toxic.[210] The practice of spraying cattle with 0.5% emulsions of DDT for hornfly control results in its appearance in the milk to an average content of 0.22 ppm. A single spraying with 0.4% suspension caused the appearance of DDT in the milk at an average level of 1.3 ppm for the following 5 weeks.[40] The substitution of methoxychlor or pyrenones for sprays on dairy cattle is therefore encouraged. However, the spraying of barns with DDT, provided cattle and their food and drink are removed, can be performed without contaminating the milk at all.[104a]

DDT may be stored in the tissues at a very low level of intake; the concentration in fat is magnified from 6 to 28 times the dietary concentration.[134a] Female dogs which had been fed 80 mg/kg daily for 443 days showed 390–670 ppm of DDT in their body fat, and secreted milk which contained 40–60 ppm.[238] Cows fed 50 mg/kg daily for 5 months showed 400 ppm in their fat and 44 ppm in their milk, which was sufficient to cause anorexia and loss of growth in rats to which it was fed. Cows fed 18 mg/kg daily on silage gave milk which had no effect on rats.[59] Cows fed silage containing 500 ppm of DDT (such that the average level in the mixed diet was 60–100 ppm) for 5 months showed 200 ppm in their fat and 1–15 ppm in their milk; this exerted no effect on rats, nor on the cows' own calves, which accumulated therefrom 300 ppm of DDT in their own fat. Sheep, similarly fed, also successfully had young, and the lambs' fat

accumulated up to 43 ppm from the mothers' milk.[230] Cows fed throughout the winter on hay containing 84–184 ppm of DDT secreted enough DDT in their milk to cause weight loss of steers drinking it, and to be accumulated by suckling calves to the extent of 825 ppm in their body fat (see Table 5). When rats were maintained over a period of years on a diet containing only 1 ppm. DDT was still stored up to 30 ppm in the body fat.[130a] *

DDT residues. The amount of DDT adhering to plant surfaces or absorbed into plant tissue may be sufficient to involve a hazard to the human consumer by chronic poisoning. Of course, this does not apply to root crops such as potatoes and onions, or to instances where only the seed is eaten and not its protective envelope, such as peas and corn and cereals. When peas are treated with 40 lb/acre of 5% DDT dust, the foliage carries 2–6 ppm of residue, but the shelled peas are free of the insecticide.[230] When sweet corn has been dusted 3–4 times with 1 lb/acre of DDT, the kernels contain between 0.1 and 1.6 ppm, as against 4 ppm in the whole plant as used for silage.[59] In many cases, the DDT is applied when the fruit is small, and a sufficient time elapses before harvest for the residue to be diluted by growth of the fruit and to be lost by weathering. Thus in green beans the fruit may carry a deposit of only 3 ppm (weathered from an initial deposit of 11 ppm 3 weeks earlier) whereas the surrounding foliage carries more than 200 ppm of DDT.[143] With lettuce, whereas a single dusting can increase the residue by 175 ppm, the residue from 2 dustings with 3% DDT decreases to 12 ppm in 3 weeks.[59] With olives sprayed with 0.125% wettable powder, the residue present at harvest 10 weeks later is only 2.5 ppm on the fruit, as compared with 185 ppm on the foliage.[173]

With apples, a residue from 0.125% wettable powder applied at the rate of 500 gal/acre takes 2–4 weeks to weather away.[59] Three weeks after the last spray, the residue on apples was found to be 2.5 ppm, on peaches 5–6 ppm, and on grapes 4 ppm. When stickers were used in the spray, the deposit on apples and peaches exceeded 7 ppm.[79] Apples and peaches purchased on the market were found to carry residues ranging up to 12 and 25 ppm respectively.[39] It is particularly difficult to remove DDT residues

* Where it may inhibit cytochrome oxidase [Editorial, *J. Am. Med. Assoc.*, **145**:735–736 (1951)].

from the surface of apples, since all the required solvents injure the fruit, and mechanical scrubbing has no effect in reducing deposits under 10 ppm;[222] DDT residue removal is therefore not practised. With grapes, residues of 7.5 ppm were found to weather down to 3 ppm in 18 days, and the deposits from 3 successive treatments of 5% dust decreased to below 2 ppm in 40 days.[173] The juice from DDT-treated grapes was found to contain nothing detectable by chemical analysis.[213a] A tentative tolerance figure of 7 ppm had been set for DDT residues on fruit by the Food and Drug Administration of the United States and the Agricultural Research Council of the United Kingdom.[87] However, the former organization now favours a limit of 5 ppm, following the conclusion of Lehman that a hazard exists if a single dietary item contains 5 ppm or more of DDT, and if a large part of the diet contains 1 ppm or even less.[69]

The entire vegetative portion of certain crops, such as alfalfa, peas, and corn, may be used for silage, which is later fed to livestock as part of their winter diet. Alfalfa taken just after an application with 3% DDT dust at 30 lb/acre carries a residue of 120 ppm, which declines to a base level of 40 ppm in a month, beyond which there is no further decrease.[73] When harvested and ready to put in the silo, corn silage dusted by current methods contains 4 ppm[39] and pea silage 2–6 ppm.[230] This DDT content decreases during ensilage fermentation to about 25% of the initial level in 6 months.[230]

TABLE 5. Transference of DDT from Diet to Cow's Milk and to Sucklings

Dietary Level, ppm	Milk Content, ppm	Storage in Body Fat of Suckling Calf, ppm
84–184 on hay[39]	Up to 25	825
60–100 on silage[230]	1–5	300
8–19 on silage[42]	Up to 0.5	...
7–8 on alfalfa hay[195]	2.3–3.0	...
5 on silage[59]	None detectable	...
1 on pea silage[230]	None detectable	...

The danger of DDT residues on hay and ensilage subsequently fed to dairy cattle is that the insecticide is transferred to the milk (see Table 5). Pea vines treated with 0.5 lb/acre of DDT in emulsion and carrying residues ranging up to 51 ppm gave en-

silage containing 8–19 ppm; cows fed on this material for 2 months yielded milk with a DDT content ranging up to 0.5 ppm.[42] Pea silage, from crops dusted at the normal rate and containing residues of less than 1 ppm, gave no contamination of the milk.[230] Cows secreted no detectable DDT in the milk even when the silage contained 5 ppm.[39] The milk from cows fed on clover hay that had been dusted 4 times with 5 lb/acre of DDT contained up to 0.9 ppm. Butter made from this milk might be expected to contain 26 ppm of DDT, well above the tolerance limit.[183] The milk from cows fed on alfalfa that had been sprayed, 10 days before cutting, with 0.25 lb/acre of DDT contained between 2.3 and 3.0 ppm, and the butter made from this milk was found to contain 65 ppm.[195] The figures in Table 5 indicate that although the DDT content in the milk is but a fraction (less than one-tenth) of the level in the diet, it may accumulate in the body fat of sucklings to a level several times higher than that in the original forage source. The use of DDT is therefore prohibited on crops to be used for winter feed of dairy cattle, and the sale of milk which contains demonstrable amounts of DDT has been banned in the United States.

There is also the hazard of transference of DDT from livestock forage to meat and eggs. Hens raised on a diet containing 310 ppm of DDT laid eggs carrying a residue of 180 ppm. Pigs fed on a ration containing 5 ppm yielded lean meat with 2 ppm and fat with 16 ppm of DDT. Steers fed throughout the winter on hay containing 84–184 ppm of DDT accumulated 9–40 ppm in their lean meat, even after a month of spring pasture. The contamination could not be eliminated from the meat by any normal cooking procedure, whether roasting, frying, broiling, or pressure cooking.[41]

Human toxicology. A total of 14 deaths from poisoning by DDT are recorded.[45a] The majority of the cases are due to accidental ingestion of the insecticide, usually dissolved in an oil base. In many of them, such as the accidental death of a woman and the suicide of an old man, the exact quantities involved are unknown.[202] In one case, a man drank a quantity of 20% concentrate in methylcyclohexanone equivalent to a dose of 500 mg/kg of DDT; death occurred in 1 hr, autopsy revealing congestion of lungs and gastrointestinal mucosa.[22] In an-

other case, a West African child drank 1 oz of a 5% solution in kerosene, equivalent to a dose of 150 mg/kg; after coughing and vomiting, she collapsed in 2 hr and died of respiratory failure (with pulmonary edema) in 4 hr.[108] Although there is a possibility that 1 oz of kerosene alone could be lethal,[17] evidence from parallel experiments on baboons indicates that this was a true case of DDT poisoning,[107] and on this basis the lethal dose of DDT for man has been set at 150 mg/kg when enhanced by solution in kerosene.[35] In yet another case an elderly man drank 120 cc of a kerosene-base fly spray containing 5% DDT, 2% *Lethane 384 Special*, and 7% xylene. He vomited repeatedly, but apart from spasms of the hands there were no tremors. He died 7 days later, and post-mortem examination showed severe necrosis of the liver and tubular degeneration of the kidneys, symptoms which could have been caused by either DDT or kerosene alone.[194] There are two additional cases of DDT being taken orally dissolved in a non-toxic oil base; the dosage levels were low and no serious symptoms were observed. (i) A healthy man ingested 1.5 gm dissolved in butter, equivalent to a dose of 20 mg/kg; the only symptom observed was the appearance of subcutaneous haemorrhages at points where the skin was submitted to pressure.[202] (ii) The experimental ingestion of 11 mg/kg of DDT in olive oil by a man gave no detectable symptoms.[155]

There are several instances of undissolved DDT being ingested; the exact dosage levels cannot, however, be established. (i) A labourer chewed a plug of tobacco which had accidentally become impregnated with DDT; within 2 hr he felt nausea, nervousness, stiffness, and a pain in the jaws; his throat remained sore for 2 days.[191] (ii) A detachment of 72 men of the Indian Frontier Constabulary made a meal of rice which happened to contain 16% of DDT; 1 hr later they were vomiting, purging, and suffering from vertigo, their pupils were dilated, and their pulse slowed, but no fatalities occurred.[213] (iii) A platoon of 25 Australian soldiers was served pie in which DDT had been accidentally substituted for baking soda; within 1–2.5 hr all the men felt giddy and weak, but only 4 vomited; only 2 required hospitalization, and they recovered in 2 days.[142] (iv) On a bet, an officer partook of 6 pancakes in which DDT had been deliberately

substituted for the flour; he not only survived but professed to have felt no ill effects.[132]

Quite a high percentage of human beings will show dermatitis when first contaminated with solutions of DDT in kerosene. This resembles a simple kerosene rash,[31] and it is considered that the dissolved DDT enhances the effect. Habituation to the solution will result in the eventual loss of this skin sensitivity.[31]

There are five instances of symptoms of poisoning induced by the contact of dissolved DDT with the skin or eyes. (i) A sprayman, whose right hand was daily soaked in a 5% solution of DDT in diesel oil, first experienced numbness and asthenia of that member, as well as a headache; he later developed a temperature of 101° F and vomited at night.[112] (ii) Two men lived for 2 days in a 6 × 6 × 6 ft chamber whose walls had been painted with DDT distemper and lube oil; where their naked backs had pressed against the walls they experienced skin anaesthesia, and they developed pains in the joints, muscular tremors, asthenia, and impairment of sight, and remained in poor health for 1 month.[13] (iii) A laboratory worker, who had kneaded an acetone solution of DDT in inert dust for some minutes, later developed nervous tension, insomnia, and aching of the limbs, with very occasional muscular tremors; he required hospitalization for 10 weeks and did not fully recover for 1 year.[229] (iv) A man engaged in formulating DDT was hit in the eyes by a mechanical explosion of the powder; he experienced intense pain for 2 days and blindness with headache for 2 weeks, but thereafter he completely recovered.[112] (v) A case of agranulocytosis of the bone marrow in a young man, resulting in a reduced production of leucocytes, high temperature, a sensation of chill, ulcerated tongue, and sore throat, was associated with his having contaminated a cut hand with the contents of a "Freon"-DDT aerosol bomb 10 days previously.[239]

Severe reactions to DDT that were possibly allergic have been reported in 6 cases, 2 of which were fatalities. Both victims were in the prime of life; one had worked in a room sprayed with 6% DDT in kerosene,[109] the other in a barn sprayed with DDT and lime.[45a]

In marked contrast to these unusual cases, there is a large body of evidence obtained under exact conditions on a great

number of men which testifies to the low level of hazard involved in the use of DDT. (i) Exposure of 2 men to an aerosol concentration of 1 gm/1000 ft^3 of DDT for 1 hr every day for 6 days resulted in no abnormal symptoms being detectable.[151] (ii) The daily swabbing of arms and hands with DDT emulsion at an area dosage of 200 mg/ft^2 and the inhalation of 100 mg daily for 1 year, by the same single subject, elicited no symptoms whatsoever.[77] (iii) Inunction of solutions, emulsions, or pastes of DDT in oils or acetone on the hands and forearms of 62 men, performed up to 10 times daily for 3 days, gave no observable symptoms and the urinalyses were normal.[55] (iv) Engagement of a working party of 15 Sinhalese in spraying the interior of warships with 5% DDT in kerosene for 9 months, using no protective clothing and even discarding normal clothing, left all men fit and happy, with no symptoms at all, not even on analysis of blood or urine.[201] (v) Underwear impregnated with DDT elicited no complaints of dermatitis in the Allied armed forces, and detailed examination of 52 subjects showed it caused no symptoms.[36] (vi) Laboratory and field workers handling large volumes of DDT dusts, also aerosols and smokes, have reported no symptoms of poisoning.[36]

From these data it is evident that DDT is one of the safest insecticides at present available for human use. When allowances are made for the toxicity of the solvent and the psychic and environmental conditions of the human subject, it will be realized that the toxicity hazard of DDT by inhalation or skin absorption is low indeed. Nevertheless skin poisoning is possible, and some individuals may show idiosyncratic susceptibility. An attempt has been made to draw up a syndrome of symptoms observed in patients who have had close contact with DDT—sore throat, nausea and other gastric trouble, pains in joints, nervousness and headache, and fine tremors—and to synonymize it with that of virus X, whose etiology has not yet been discovered.[24] DDT can be toxic by the oral route, since its cumulative action introduces a material hazard of chronic poisoning. Although a human subject took DDT in his drinking water for a year (water dusted at 300 mg/ft^2) and confessed to no ill effects, it is possible he may have suffered liver damage.[77] But this type of pathology, caused by low levels of dietary DDT, is rapidly

rectified when the compound is no longer present. There remains the danger that DDT from various dietary sources may be fixed in cow's milk or mother's milk. Although the concentrations are no higher in milk than in the original sources, the DDT has been transferred to a principal, if not the exclusive, dietary item of a young and unusually susceptible mammal.

DDD

Dichlorodiphenyldichloroethane, or TDE, is only one-tenth as toxic as DDT,[1] the oral LD_{50} to mammals being approximately 2500 mg/kg. An oral dose of 3000 mg/kg induces moderate neurotoxic symptoms in rats, followed by death in 1–12 days.[193a] The dangerous level of inunction is 2800 mg/kg, and multiple applications of 100 mg/kg of this slightly irritating material can be tolerated.[134] Cows, pigs, horses, sheep, and goats show no symptoms on being sprayed many times with 1.5% emulsions of DDD, and calves are unharmed by a single exposure to 8% emulsions.[30]

The chronic toxicity of DDD is $\frac{1}{25}$ that of DDT, the dietary level at which animals begin to show gross effects being 2500 ppm.[134] DDD gives rise to DDA in the urine. Domestic fowl are more susceptible, 100 ppm of DDD in the diet proving lethal to some chickens within 30 days; the same amount of DDT killed all chickens in 10 days. The DDD-poisoned fowl showed subcutaneous and pericardial edema.[211] When dogs were fed daily doses of 50–80 mg/kg, half of them were still surviving after 21 months. Autopsy revealed a damage to the liver comprising atrophy, necrosis, cirrhosis, and fatty degeneration; and the DDD had produced a distinctive and almost unique symptom—a marked atrophy of the adrenal cortex.[156]

Methoxychlor

Dimethoxydiphenyltrichloroethane, or methoxy-DDT, has a very low level of acute toxicity by mouth, the LD_{50} being about 7000 mg/kg for rats,[193a] and over 6000 mg/kg for mammals in general.[134] The course of poisoning in rats is marked by diarrhoea, progressive weakness, and death within 2 days.[193a] The dangerous level of inunction is 2800 mg/kg, and multiple applications of 600 mg/kg of this slightly irritating material can be

tolerated. Livestock are unaffected by 1.5% emulsions repeatedly applied, and calves withstand 8% emulsions.[171a]

Steers are unaffected by a single dose of 500 mg/kg of methoxychlor, and sheep withstand a single dose of 2000 mg/kg or daily doses of 100 mg/kg; at these levels DDT always induces marked nervous symptoms.[226] After 15 daily doses of 200 mg/kg, rabbits show diarrhoea and anorexia, and in some cases they develop fatty hearts and livers.[195] The chronic dose of methoxychlor at which animals start to show gross effects has been put at 5000 ppm; it is not surprising that the effect is kidney damage.[134] The growth rate in rats is normal on diets containing up to 1000 ppm.[109a] Methoxychlor shows little tendency to be stored in the body fat.[241] Neither methoxychlor nor its acetic acid derivative is to be found in the urine; it is suggested that the molecule is more profoundly metabolized, its anisole groups being converted to hydroxyphenyl derivatives.[161]

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CHAPTER VIII

Toxicity of Insecticides to Plant Growth

Fumigants

Hydrogen cyanide. In the dosages required to kill insects, HCN is quite safe for use on plants. Growing citrus trees have been fumigated for years without injury, the exposure period under the tent being 45 min, during which time the dosage falls from 4 mg/litre to 0.2 mg/litre. This is done at night, for severe foliage and fruit injury results unless the trees have been totally free of sunlight for at least 1 hr, or if they encounter sunlight immediately after the fumigation is completed. In greenhouse fumigation with calcium cyanide at 0.75 oz/1000 ft^3 (equivalent to 0.13 mg/litre of HCN) for 3 hr, certain varieties of carnations develop whitened areas on sepals and leaves;[21] the susceptibility is heightened if the soil is damp and the plants are not shaded after treatment.[48]

The effect of HCN on tomato is to cause epinasty and hyponasty of stem and petioles, and is quite independent of the slight *p*H change induced in the sap of the plant. At a vapour concentration of 1000 ppm, stem injury occurs in 15 min in tomato and tobacco, and in 60 min in buckwheat; leaf injury appears in 12 min in tomato and buckwheat, and in only 4 min in tobacco.[177] Hydrogen cyanide does not affect the capacity of seeds to germinate but may delay germination.[18] It is scarcely toxic to active stages of pathogenic fungi,[122] nor is it absorbed on foods enough to constitute a hazard to the consumer.[51a]

Hydrogen sulphide. Hydrogen sulphide vapour is only slightly toxic to plants. The youngest shoots are much more susceptible than mature foliage and may be completely scorched, whereas in older leaves this scorching (necrosis) is limited to the margin and base of the leaf. Cucumber, tomato, and tobacco are susceptible, showing slight injury at 40 ppm; while apple, cherry, and peach are moderately resistant, 400 ppm being required for any injury to appear.[121] At a concentration of 1000 ppm, leaf injury in the tomato appears after 30 min, stem injury after 45 min.[177]

Hydrogen sulphide may be considered to be the causative agent in foliage injury by lime-sulphur with its associated polysulphides. Acute injury by lime-sulphur involves the scorching of tips and margins of young leaves, and necrotic patches adjoining the larger veins of older leaves. Chronic injury is characterized by a premature abscission of leaves and fruit. This effect of lime-sulphur may reduce the apple crop by at least one-half.[118] Severe injury has resulted to pear foliage when application has been made at high temperatures and in drying winds,[137] and apple foliage has been damaged by lime-sulphur or wettable sulphur at high temperatures.[76] It has been considered that phytotoxic hazard enters when temperatures exceed 26.5° C. Severe leaf injury may result if summer-oil emulsions are combined with lime-sulphur or wettable sulphur.[109] Hydrogen sulphide does not reduce germination but may delay it.[122]

Sulphur dioxide. This penetrating, water-soluble, and acid gas is very toxic to plants. A vapour concentration of 1 ppm is sufficient to injure most plants after 1- to 7-hr exposure; buckwheat is most susceptible, and orchids comparatively resistant.[191] Tomato plants exposed to 1000 ppm develop leaf injury in 1.5 min and stem injury in 22 min; the acidifying action of the SO_2 at this concentration reduces the *p*H of the leaf tissue from the normal 6.0 down to 4.0.[177] The first symptom of injury is the appearance of pale areas between the veins of the leaf. Buds and unfolding leaves are more resistant than mature foliage; plants are less susceptible in the dark.[191] Sulphur dioxide reduces or delays the germination of seeds, although the dry seeds of some plants are resistant.[18] It is highly toxic to fungi pathogenic to plants.[122] Thus it is effectively used on fresh fruits.

such as grapes, to reduce spoilage from the growth of micro-organisms and moulds.[48]

Carbon disulphide is sufficiently non-phytotoxic to be used as a soil fumigant, although at high concentrations it has been employed to kill perennial weeds.[48] It may endanger the germination of moist seeds, but not of dry seeds. Fresh fruits have been fumigated by CS_2 without injury; dry fruits will remain tainted unless thoroughly aired after fumigation.[135]

Chloropicrin is a non-contaminating fumigant for grains and flour and for dried and fresh fruits. It has also been used as a seed fumigant, although it has been reported to injure the germination of alfalfa and radish. It is an effective fungicide and bactericide.[48]

Ethylene oxide has been found to affect seriously the germination of wheat.[37] At a concentration of 2 lb/1000 ft^3 (= 32 mg/litre) it has no effect on dried fruits or nuts, leaving no taint; this concentration is also safe for fresh fruits, except that it severely injures bananas.[135] Ethylene oxide leaves no taint on grain nor does it change its milling properties.[15]

Ethylene dichloride is safe for seed fumigation, having no deleterious effect on germination. However, it taints fatty foodstuffs.[48] It has been used as a soil fumigant for peach-tree borer control and has caused injury on application in the autumn when the soil is wet and cold.[158] Certain soils are more liable to promote injury than others: in sandy soils, peach trees will tolerate as much as 4 oz of 30% emulsion, and the cambium flecking that appears with 70% emulsions is transitory.[163] When applied to turf at the rate of 1 gal of 1% emulsion per sq yd, ethylene dichloride causes a slight yellowing of the grass but no permanent injury.[119] Propylene dichloride applied to the soil at 290 lb/acre with a soil fumigator did not damage a variety of crop plants subsequently planted in it.[129]

Methyl bromide. The phytotoxicity of this favoured fumigant first begins to appear on the growing tips and on the roots. Vapour concentrations of 1 lb/1000 ft^3 are safe for most growing plants in greenhouses, provided access to the roots is prevented by a prior watering of the soil.[146] Non-dormant rose plants are susceptible; 6 varieties were found to exhibit necrosis of the growing tip and the region below the new buds when exposed to

concentrations above 0.25 lb/1000 ft^3. Ornamental conifers are susceptible to methyl bromide injury in late spring, when their metabolism becomes highly active, but not in the winter, when they are dormant.[110] Peach nursery stock may be safely fumigated with 2 lb/1000 ft^3 (32 mg/litre) for 4 hr when in a dormant condition; higher concentrations cause tip injury.[98] Dormant strawberry plants withstand exposure to 3 lb/1000 ft^3 for 3 hr and show a stimulation of growth when subsequently planted; [105] non-dormant plants are severely damaged by this concentration.[147] Nursery stock of camellias is resistant to this latter dosage, but 2 varieties of azaleas (out of 79 tested) proved to be susceptible to injury. The hazard of methyl bromide injury to nursery stock is enhanced by an increase in temperature and light conditions[58] and is inversely proportional to the transpiration rate of the plant during the 6-hr postfumigation period.[5] This fumigant is harmless to the germination of seeds of legumes or cereals, and of seed sweet potatoes,[52] in concentrations up to 160 mg/litre.[60]

Methyl bromide is a safe fumigant for fresh or dried fruits, and the slight taint dissipates quickly. However, fumigation of tomato and papaya fruits at 2.5 lb/1000 ft^3 was found to delay ripening and increase their susceptibility to anthracnose injury.[48] At this dosage level the skin of oranges becomes deeply pitted, no other citrus fruits showing this injury.[12] Most varieties of stored apples are resistant to this concentration, but Jonathan and McIntosh develop internal and external injuries.[138] The Williams variety is the most susceptible of all, showing surface scald and internal browning at doses which are harmless to any other apple or peach.[101] If the dosage of methyl bromide is raised to 3 lb/1000 ft^3 and maintained for 6 hr, almost all kinds of fruit are injured.[97]

Methyl chloride, used in aerosol bombs in greenhouse work as a more readily compressible substitute for "Freon," has proved to be more hazardous for plants than the dichlorodifluoromethane it replaces. **Ethylene dibromide** is used as a soil fumigant without injury to the growing plants. Continuous exposure of seed grain to 100 mg/litre for 9 months has had no effect on germination, although a slight effect begins to appear at 200 mg/litre.[illegible] The soil should be fumigated either when the plants are dormant,

or in advance of seeding. **Acrylonitrile,** a "spot fumigant," proved harmless to seed germinability at doses up to 12.5 lb/1000 ft^3.[71] **Trichloroacetonitrile,** the European fumigant, has no effect on the germination of wheat when employed at 3 lb/1000 ft^3.[30] **Paradichlorobenzene,** used as a soil fumigant for borers at the base of peach trees, has proved harmless if applied as crystals.[188] However, when applied in oil emulsion in late summer it may prove injurious, trees treated in early September in Canada having been severely injured, with 25% succumbing.[13] A dosage of 4 oz of PDB per tree may cause flecking of the cambium or wood, but the tree as a whole may be unharmed.[163] The fumigation of seed sweet potatoes with PDB retarded their germination.[52]

Mineral oils

Owing to their comparatively low surface tension, petroleum oils readily enter the stomata of leaves,[182] whose orifices measure approximately 20 μ by 5 μ in apple foliage.[189] They may also penetrate directly through the epidermis. The greater amount of penetration occurs on the leaf undersurface, where the stomata are most abundant.[48] In citrus foliage, oil readily penetrates both sides of the leaf.[151,189] In apple and peach only the less viscous oils penetrate the upper surface of the leaf,[70] which is resistant to the heavier oils.[179] When oil is sprayed on foliage, it passes through the stomata into the intercellular spaces of the leaf, and thence into the vascular bundles and the parenchyma cells. Passing along the tracheae which constitute the vascular system of the leaf, it is translocated into the twigs and deposited in the pith and xylem parenchyma.[107,189] The speed of entry is inversely proportional to the viscosity of the oil,[70] which in turn may be modified by the temperature.[190] Kerosenes penetrate into the vascular system within a matter of hours and are readily translocated as globules of oil. More viscous oils may require several days to penetrate and be translocated, or they may clog the vascular system and thus decrease or stop translocation entirely.[48]

The filling of the intercellular spaces of the parenchyma with oil retards the gaseous exchange of the leaf.[151,189] Carbon dioxide will accumulate and oxygen fail to reach the active cells; in apple

fruit the presence of oil halves the oxygen tension and raises the CO_2 content from the normal 18% up to an abnormal 25%.[28] Oils applied to unfolding and active foliage reduce the rate of respiration,[107] whereas dormant oils applied to twigs and buds increase it.[48] The starch produced in the apple leaf is correspondingly reduced;[28] with heavy applications starch production may cease altogether, not to resume until the oil has been largely eliminated, while light applications cause a retardation comparable to a spell of cloudy weather. The decrease in starch production results in a stunting of the crop and of the next year's buds.[48] The transpiration rate is also reduced.[102, 107] The mechanical presence of the oil does not in itself kill leaf tissue, since plant cells can live indefinitely in medicinal paraffin.[40] The application of 2% emulsions of medicinal paraffin (*Nujol*) is quite harmless to the foliage of apple and peach.[69] However, the mechanical effect in blocking the vascular system may accelerate the drop of old leaves and ripe fruits.[49]

The ingredients of the oil that kill plant tissue are the unsaturated olefins, aromatic ring structures, phenolic groups, and sulphur compounds (principally mercaptans) that are present in inadequately refined petroleum oils.[49] The mercaptans injure foliage almost as soon as they are applied. Benzene is highly phytotoxic, and the toxicity rises with increasing substitution of alkyl groups.[40] The naphthenes are less toxic, cyclohexane being more inert than cyclohexene. Although saturated paraffns are not phytotoxic if they evaporate off the plant within a short period of time, the presence of double bonds renders them toxic.

The content of unsaturated compounds, aromatic as well as aliphatic, is measured by the percentage of the oil which may be removed upon sulphonation with liquid SO_2 or H_2SO_4. What is left, i.e. the unsulphonatable residue, is made up of the saturated compounds. Thus the unsulphonatable residue (U.R.) which may be found in an oil is a measure of its purity with respect to freedom from unsaturates. It has been found to be also a measure of the blandness of the oil to plants. On the other hand, the amount of sulphonatable material in the oil is a measure of its phytotoxicity. When used in 5% emulsions on orange trees, kerosenes were non-toxic if they had less than 16% sulphonatable material and comparatively safe if less than 25%; they were

moderately toxic if the content was over 25%, and very toxic if the sulphonatable material exceeded 40%.[79] It was found with the apple variety Hibernal that oils were dangerous to foliage if they were more than 15% sulphonatable, and to buds if more than 45% sulphonatable.[190] Gasolines applied to cabbage showed much greater toxicity if they were cracked, which implies a high content of unsaturates, than if they were straight-run.[40] A grade of light lube oil, which in an unrefined state defoliated peach when applied in 0.25% emulsion, when refined gave no leaf drop even in 0.5% emulsion.[68] The foliage of plum, peach, and apricot is severely injured by an 83% U.R. mineral oil; translucent spots appear which become brown, and the leaves may turn yellow and fall; apricot is the most susceptible. With a 93% U.R. oil, the translucent spots appear but no leaf fall occurs, and with a highly refined oil there is no injury at all.[133] Whereas petroleum distillates of 50–60% U.R. caused leaf burn, defoliation, twig kill, and fruit scar of orange trees, a highly refined oil of 98% U.R. of about the same viscosity grade (approx. 100 SSU) gave no injury to foliage, twigs, or fruit.[49] The refined oils—i.e. odourless kerosene, mineral seal oil, and medicinal paraffin, in ascending gravity—show no acute toxicity to foliage of orchard crops or field plants.[40, 68, 179] On the other hand the materials which were removed from the respective crudes in the refining process, the so-called Edeleanu extract containing the sulphonated unsaturates, are highly phytotoxic, the aromatic fraction being worse than the olefinic. Isoparaffin, built up by polymerization to contain no olefins or aromatics, is scarcely toxic even to the sensitive barley plant.[40]

A distinction is made between the acute toxicity to plants, which appears within 2 days of application, and a chronic toxicity, which may take some weeks to appear. Acute toxicity is inflicted by the lighter, less viscous materials such as benzene and xylene, or unrefined aliphatic oils with molecules ranging up to C_{16}, i.e. the kerosenes and lighter stove oils and fuel oils. In hot weather, even the heavier fuel oils may be sufficiently non-viscous to cause acute injury (Fig. 1). When acutely poisoned by such materials, the leaf tissue may become "burned" to a brown colour, due to discolouration of the chloroplasts, and the essential odours

may be released; [40] or the leaves may drop before discolouration appears, as happens in citrus foliage.[19] Acute damage by oils may appear in apple foliage as brown or purple necrotic spots or areas, or silvery and translucent chlorotic spots or areas, on the undersurface of the leaf. Certain of the most toxic oils promote the appearance of purple spots on the upper surface of the leaf also.[190] The poisoned leaves may be stunted in their subsequent growth or may fall prematurely.[189]

Fig. 1. Acute toxicity to lupin foliage of unrefined No. 2 fuel oil. (Courtesy of Division of Entomology, Department of Agriculture, Canada) The chlorotic spots mark the positions of coarse droplets from an aircraft spray.

However, since these materials are also more volatile, chronic toxicity does not develop once the acute period is passed and they have evaporated off. Nevertheless most kerosenes and the heavier stove oils may show chronic toxicity. The various species of plants show marked differences in their susceptibility to acute poisoning, the umbelliferous species such as carrots, parsnip, celery, and parsley being especially resistant, and grass and

cereals being rather susceptible. This varietal specificity is not evident in chronic poisoning by oils.[40]

Chronic toxicity may take weeks to develop; in citrus the foliage turns yellow, there is a slow, steady leaf fall, and the twigs and branches become stunted or killed.[49] In grasses a general chlorosis (yellowing) sets in, the haulms are stunted, the meristems may be killed, and mildew infection may ensue.[40] Chronic toxicity is caused by diesel oil, fuel oil, lube oil, and the heavier kerosenes and stove oils. If kerosene is used as a solvent for DDT and applied at 10 qt per acre, it decidedly injures the foliage of field crops, and particularly squash. *Velsicol AR-50* applied at 2 fl. oz. per acre in emulsions is moderately injurious, whereas *Amsco-Solv A*, like xylene, caused no foliage injury.[89a]

TABLE 1. Injury to Young Barley Plants by Petroleum Oils [40]

Percentage injury from foliage-wetting sprays

Type of Oil	Days after Spraying					Injury
	1	2	4	7	9	
White gasoline	60	100	100	100	100	Acute
Stove oil	75	100	100	100	100	Acute
Diesel oil	30	75	95	100	100	Chronic
Odourless kerosene	0	10	25	100	100	Chronic
Heavy isoparaffin	0	0	5	20	40	Chronic

In the unrefined oils the toxicity is due to the sulphonatable impurities already mentioned as responsible for acute toxicity. But even refined oils, such as mineral seal oil, heavy isoparaffin, *n*-cetane, and the heavier odourless kerosenes, may eventually show chronic toxicity (Table 1). This is considered to be due to the secondary formation of asphaltogenic acids which have acquired —OH or —COOH groups. A concentration of 0.5% of these acids in an oil is sufficient to injure peach foliage.[179] These refined oils also may gain phytotoxicity if stored in containers allowing the entrance of light. The oxidative change takes place at the unsaturated double bond, with the initial formation of

peroxides and their conversion to acids. It requires free oxygen and radiant energy, ultra-violet light being particularly active. Saturated paraffins oxidize very slowly indeed. Whereas aromatic oils start to oxidize immediately on exposure to light, paraffinic oils show a latent period of little change and then oxidize at a significantly higher rate.[93] Refined distillates are considered to be particularly susceptible to this change because of the removal of the natural antioxidants in the refining.[10] The reaction may take place not only on the surface of the plant but also within it, where there may be available a supply of reactive oxygen produced during photosynthesis.[93]

If the distillates are light and sufficiently volatile, this type of chronic toxicity cannot develop. The danger of chronic poisoning increases with decreasing volatility, until the peak of chronic toxicity is reached with oils of approximately 30° Bé gravity for citrus[79] or 100–110 SSU viscosity for apples.[18,116] With heavier oils eventually the viscosity becomes so great that entry into the plant tissue is too slow to take effect before natural leaf fall supervenes. The importance of viscosity as deciding penetration may be so great as to over-ride the question of degree of refinement. When applied in 0.5% emulsions to apple foliage, a diesel oil of viscosity 1200 SSU and only 5% U.R. was no more toxic than a summer oil refined to 94% U.R. but of viscosity 77 SSU; moreover it did not cause defoliation to occur after an application of sulphur, whereas the summer oil did. With dormant oils applied to the crowns of pear trees, a California oil of 214 SSU viscosity was less toxic than similar oils of 105 or 38 SSU viscosity. When applied to trunks of apple for 6 successive seasons, a dormant oil of 200–250 viscosity killed none, and one of 100–110 viscosity killed 25%, while summer oils and fuel oils of 30–75 SSU viscosity killed 50% of the trees. The most highly toxic oil was a mid-continent oil of 110 SSU viscosity, but also of high kinematic viscosity index (A.S.T.M. Designation: D567-40T), a term meaning that for its viscosity it had an unusually high gravity and thus was unusually non-volatile.[116] Oils of a viscosity of 90–110 SSU have frequently caused defoliation of apple or stunting of the fruit.[134]

In order to be safe for application to foliage of orchard trees, the degree of refinement of summer oils must be not less than

90% if they are light; if they are heavy the safety requirement rises to 94% U.R.[48] The hazard increases as the temperature of application rises, partly because of the consequent drop in viscosity, and in hot weather even these refined oils may cause foliage burning.[9] At very low humidities the foliage is so desiccated that oils enter more readily and the chances of injury are higher.[182,190] Although the rate of re-evaporation of oil from surfaces is unaffected by the relative humidity obtaining, it has been found that very high humidities intensify the oil injury.[48] Once within the plant or tree, elimination of oil is very slow indeed.[189] The penetration of spray oils into foliage may be retarded by salts of oleic or stearic acid,[48] aluminum stearate being an effective safener for kerosene emulsions on citrus foliage.[55] The oxidation of spray oils may be inhibited by adding certain amines, disulphides, thio compounds, or phenolic or halogen derivatives as antioxidants.[93] Emulsions penetrate more slowly into the leaf than pure oil applications and exert less injury.[70] Quick-breaking emulsions may be more injurious since they leave a continuous oil film, and therefore for safety more highly refined oils[47] are demanded in this case.

Mineral oils also cause injury to the fruit. Oil penetrates the skin of the apple through its lenticels, entering the parenchyma spaces and sometimes reaching the core cavities.[189] Heavy summer oils (100–110 SSU) have caused russetting, calyx-end darkening, or brown spotting on certain varieties.[134] Even when used at safe dosages on apples, summer oils spoil the "finish" of the fruit. The size of the apple is reduced,[134] though this may be a secondary effect of lowered starch formation in the foliage[48] or of interrupted translocation. Heavy oils have been found to retard the growth of plums at the ripening period.[48] Citrus fruits may be affected by oils, which can give rise to skin roughness or inhibit the development of the ripe colour; sometimes the fruit is scorched or drops prematurely. Possibly as a secondary effect of foliage injury, the sugar content and flavour of the fruit are impaired, and its susceptibility to decay in wet weather is increased.[151]

The trees themselves may be irreversibly injured by oils. In the apple, only the lighter oils of low viscosity can directly penetrate the corky bark and reach the cambium;[70] the heavier oils

enter by translocation from the foliage. With dormant oils, buds may be killed and the twigs may die back from the tips. Narrow canker lines will develop in the bark separating the dead cambium from the living, and yellow or gray blisters may appear.[189] On citrus trees, oils may kill the cambium of the twigs and the injury may be shown in the adjoining bark or xylem. On larger limbs quite considerable areas of inner bark may be killed.[151] The trunks may be completely girdled by the toxic action of lighter fractions of kerosene which may have accumulated just below the surface of the soil.[54]

Animal and vegetable oils. When applied in the 2% emulsions commonly used for summer application to orchard trees, these natural oils prove to be not only more expensive but usually more phytotoxic than refined petroleum oils. Only sperm oil was found to be harmless at this concentration. Fish oil, castor oil, olive oil, pine oil, and turpentine all caused foliage injury to apple or peach.[69] Seal, corn, and peanut oils have proved to be injurious to peach and apricot foliage under certain conditions.[133] Pine oil applied at 2 oz/acre in DDT emulsions proved moderately injurious to field crop foliage.[89a]

Soaps and other detergents. In the low concentration necessary to reduce the surface tension of aqueous sprays, soaps are harmless to foliage. The soft soap of coconut oil (mainly potassium laurate) proved to be harmless to many species of plants when applied in 0.25% solution. If the concentration was raised to 2.0%, it injured most of the plants, the most susceptible part being the blossom.[72] There is evidence that soaps may render oil emulsions injurious to plants, where neither oil nor soap alone had been toxic.[57]

The modern synthetic detergents, mainly alkyl aryl sulphonates, are components of the emulsion concentrates and wettable powders of organic insecticides. The addition of certain detergents to DDT dusts has been found to induce epinasty in tomato and chlorosis in other plants.[12] The detergents used with DDT wettable powders have been blamed for the considerable injury they have caused to elm foliage.[153] Since the kind of detergent used and its amount in commercial formulations are generally not divulged, data on the phytotoxicity of these compounds have not found their way into the literature.

Arsenicals

Soluble arsenic sprayed onto foliage is absorbed into it. Hence it is applied in as insoluble a form as possible, in the hope that sufficient will be solubilized in the gut of insects to poison them without enough becoming solubilized by weathering to poison the foliage. The margin is often narrow.[161] Arsenic is absorbed directly through the cuticle, and thus mostly through the undersurface where the cuticle is thinnest.[176] Heavy accumulation of moisture increases the permeability of the cuticle to arsenic, an effect also produced by lime. Holes in the leaf made by insects, fungi, or hail allow the arsenic to enter unimpeded and spread damage from there. However, peach foliage has been killed by Paris green without absorbing any arsenic, and it is considered that soluble arsenic can kill by direct plasmolysis of the foliage.[65] Paris green used at the low concentrations of mosquito larviciding has no effect on the vegetation in the water.[20]

High concentrations of soluble arsenic will produce acute injury, and the leaf will die and blacken overnight; this is known as arsenical burning. It is more usual to encounter chronic injury, termed yellow leaf; in the apple this generally starts as spots of red, brown, or purple, or as darkened margins, and the surrounding yellow may spread to engulf the whole leaf, which then falls. This is due to absorption of arsenic over the entire leaf lamina; it may occur only on the margins because of accumulation of spray there.[6] The soluble arsenic increases the respiratory rate of the leaf. When this increase exceeds 50%, the leaves turn yellow and drop off.[126] Older leaves are more susceptible than younger, and the basal die sooner than the terminal. Successive sprays may have a cumulative effect on leaves, even when surface deposits are washed off each time.[175a] The foliage of pomes is more susceptible than that of most shade trees. Peach foliage is very susceptible to injury by lead arsenate, showing shot-hole areas or yellowing and premature drop of the leaf;[6] for this reason lime is added as a safener in peach sprays.[112] Defoliation may also occur and may reach 75% with basic lead arsenate and 100% with acid lead arsenate, the latter damaging twigs also.[162] The spraying of sublethal amounts of soluble arsenic increases the rate of fruit maturation of citrus trees. It

has been claimed that traces of arsenic are growth-promoting for plants.[65]

This foliage injury may be increased by the use of vegetable or animal oils, but not petroleum oils.[117] Addition of soap as a spreader to soft water increases the hazard by solubilizing arsenic, although in hard water it decreases the soluble arsenic which is already present.[71] Foliage injury may be reduced by the addition of metallic oxides, which turn into the hydroxide on the leaf and adsorb the soluble arsenic;[73] ferric oxide is the most suitable since Zn or Al oxides are themselves phytotoxic.[69] Hydrated lime may greatly reduce the amount of foliage injury from lead arsenate, but its performance is erratic. Bordeaux mixture reduces arsenical phytotoxicity.[94] Lime-sulphur also has a safening action but reduces the insecticidal activity of lead arsenate, whereas zinc sulphate is a "safener" and increases it. However, a mixture of zinc sulphate and calcium hydroxide (lime) has proved a satisfactory safener[6] and is superior to hydrated ferric oxide as an additive for lead arsenate.[117] Even with zinc sulphate safener, the foliage of pomes and particularly plum[157] may suffer injury from calcium or lead arsenate applied at high temperatures (over 80° F) or under slow drying conditions.[6] Of the arsenicals used in orchards, lead arsenate is considered to be the least phytotoxic, and calcium arsenate to be the most hazardous.[145] Calcium arsenate at normal spray application rates will burn apple foliage in cool damp weather[6] and is unsafe to use at any time on peach, cherry, or plum.[142] When dusted at the rate of 40 lb/acre it will even burn the foliage of conifers.[177] Calcium arsenate is extensively dusted on cotton, and the oxides of Fe, Cu, Pb, or Zn may be used as safeners, Mg or Mn oxide being ineffective.[22] Paris green is safe to use on most field crops, and on pome fruits when lime is added, but should never be used on stone fruits such as peach, cherries, or plums.[142]

The application of an arsenical such as lead or sodium arsenate or Paris green to limbs of apple is quite harmless to the tree provided the bark is intact. But once entry is made through bark wounds, dormant buds, or lenticels, lead arsenate can injure apple twigs and branches.[176] The fine twigs of the peach may be directly burned by high concentrations of this arsenical; the

new wood exhibits necrosis, and the growth of the previous year develops cankers with the bark splitting.[83]

Under certain circumstances fruit injury may develop in apples treated with lead arsenate, despite the fact that arsenic is not normally absorbed through the skin. A condition known as "skin russet" results from the suberization of cuticular areas that have been directly killed by soluble arsenic. The red or black spots which develop have been found to contain twice as much arsenic as the remainder of the skin.[65] Blossom-end injury, which is apparent as a dark brown area around the calyx, results from accumulation of arsenic in the calyx cup.[51]

It is possible also for fruit trees to be poisoned through the roots. The first symptom is a premature yellowing of the foliage, and the tree generally dies in the following year. Patches of sunken bark and dead cambium may develop on the trunk, and complete girdling may result in death of the crown; the roots lack fine rootlets, and their bark may be destroyed; the discoloured wood may contain up to 13 ppm of arsenic. This type of damage was first reported in 1908 in isolated trees throughout the orchards of Colorado, which were heavily treated with arsenicals.[89] The damage is worse in alkaline soils which solubilize arsenic, and where certain soil microorganisms reduce arsenates to the more toxic arsenites.[65]

It is, however, likely that this type of arsenical injury is not due to direct poisoning of the intact root system. For although some orchards may collect more than 3500 lbs/acre of lead arsenate in a quarter-century, the arsenic seldom descends below the upper 8 in. of soil (i.e. as deep as it is cultivated), whereas 90% of the roots are below this level. Normal trees in such orchards are found to contain no more than 0.1 ppm of arsenic or 0.3 ppm of lead.[100] Moreover, trees may be treated around their base with heavy applications of arsenicals without harmful results; a grapefruit tree was unaffected by 30 lb of lead arsenate to give 2000 ppm in the soil,[126] and apple trees survived 15 gm of Paris green or 60 gm of lead arsenate.[176] However, if the arsenic could enter through wounds in the upper roots, whether caused by the stripping of bark or the trimming of water sprouts, injury was manifested. It is also possible that the corrosive

action of high concentrations of arsenic may eventually destroy the protective power of the bark against entry.[89]

TABLE 2. LEAD ARSENATE IN THE SOIL AND GERMINATION AND GROWTH OF CROP PLANTS [63]

Per cent reduction in soil treated at 2000 lb/acre

	Germination	Growth
Onion and tomato	Very slight	Very slight
Pea, cauliflower, Brussels sprouts, squash, and parsnip	Very slight	10–19
Cabbage, lettuce, radish, turnip, and sweet corn	Very slight	11–37
Carrot, cucumber, broccoli, and okra	Very slight	25–37
Spinach	13–22	Very slight
Beet	13–22	11–37
String bean	40	25–37
Lima bean	98	.....

When arsenic is added to the soil it becomes "fixed" or rendered insoluble, a form in which many natural soils hold much natural arsenic; most of the orchard soils contained insoluble arsenic originally. The fixation of soluble arsenic such as sodium arsenite may be completed within a day or may take weeks, and may amount to a figure between 75 and 99% of the dosage applied.[151] Fixation is much faster and more complete in clay soils than in sands, and is increased by the presence of iron in red soils. Thus it will be found that clay soils require the addition of much more arsenite to give the same degree of plant retardation. For a yield reduction of 50% in oats, sands require only 70 ppm, loams 120 ppm, and clays as much as 190 ppm of As_2O_3. The rates of fixation of arsenite by different soils, along with the level required to halve the yield, are shown in Table 2. Each successive crop renders the arsenic-treated soil less toxic, so that by the seventh cropping the plants survived in soils containing 2–5 times the dosage that killed the first crop.[41]

The reduction in yield is roughly proportional to the amount of soluble arsenic added (see Fig. 2).[41] However, very low concentrations of sodium arsenate actually stimulate plant growth. This stimulating effect is shown by peas, wheat, and potatoes at concentrations up to 25 ppm, and radishes up to 75 ppm. In-

hibition occurs at higher levels, appearing at 75 ppm in the case of beans, one of the most sensitive plants; the inhibitory level for wheat is considerably above this figure.[172] Grass is very resistant to arsenical poisoning, 7 species of grasses being uninjured by turf applications of lead arsenate at 1500 lb/acre,[82] but 3 species of blue grass were injured at 1500 lb/acre.[111] Paris green begins to injure vegetation at 900 lb/acre.[127] At 2000 lb/acre of lead arsenate, the germination of most field-crop plants is scarcely affected, with the exception of beets, spinach, string

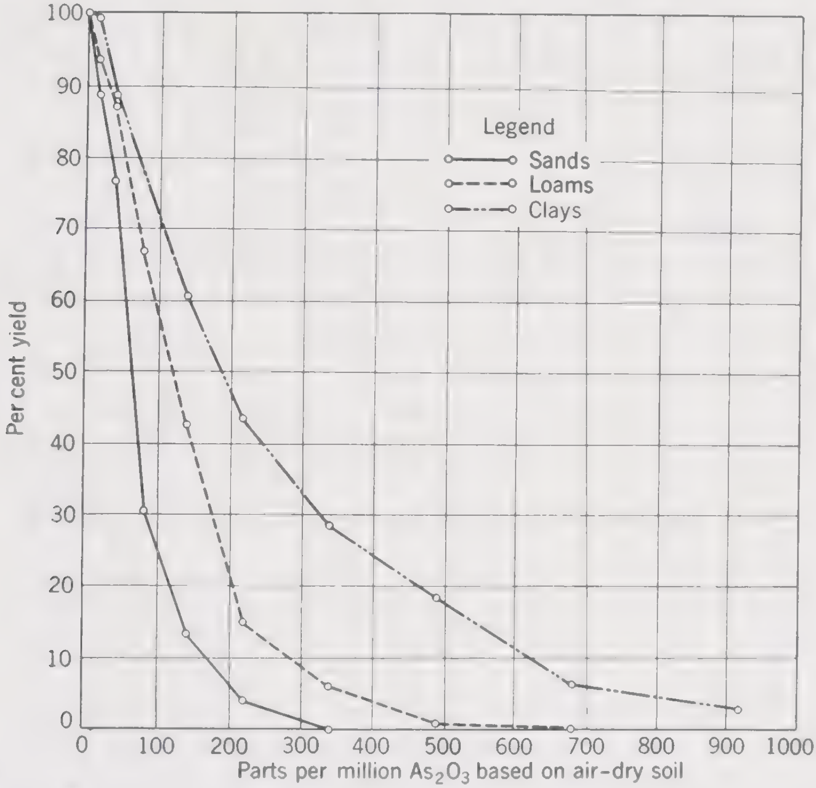

FIG. 2. Reduction in yield of oats caused by arsenic in the soil. (From Crafts and Rosenfels)

beans, and lima beans, the latter showing 98% inhibition (Table 2). While the subsequent growth of onions and tomatoes is scarcely affected at this dosage, most crop plants show a reduction in growth ranging between 10 and 37% of the normal.[93] Lima beans grown in sandy loam do not germinate at all when treated with lead or calcium arsenate at 500 lb/acre; in clay

loam they achieve a yield of 15% of the normal. At 3000 lb/acre, lead arsenate completely inhibits the growth of bell peppers, but calcium arsenate allows a yield between one-quarter and one-third of the normal.[159] At high levels of arsenic in the soil the plants may wilt, to make way for a stimulated growth of algae, moulds, and other fungi and soil bacteria.[1, 89]

The effect of arsenical poisoning through the soil seems to be the destruction of chlorophyll in the foliage.[172] Plants grown in water culture containing 1 mg/litre arsenious acid show blackening of the vascular bundles in the leaves.[4] The arsenites are decidedly more toxic than the arsenates,[38, 89, 127] and of the latter lead arsenate is the least toxic to most species. The first effect of soluble arsenite is to decrease the transpiration rate, oats responding in this way to concentrations of 1 ppm. Beans and cucumbers are very sensitive; turnip, cereals, and grasses are comparatively resistant.[127] Arsenic taken up from the soil is deposited mainly in the leaves, whereas only a small amount is found in fleshy fruits, and traces in dry fruits and seeds.[4] On the other hand, arsenicals applied to the foliage are not translocated in the roots or tubers, e.g. potatoes.[65] When crop plants are grown in soil treated with lead arsenate at 2000 lb/acre, most species take up no more than traces of arsenic; those that take up most into the edible portions are lettuce, onions, beets, radishes, and turnips, which come to contain 0.01–0.02 grain/lb of arsenic as As_2O_3.[63] When grown in old orchard soils in New Jersey poisoned with lead arsenate to the extent of 90–230 ppm as As_2O_3, most crops had little more than a trace of arsenic, whereas potatoes, squash, and cucumbers contained 0.02–0.05 ppm.[124] Onion bulbs contained 0.11 ppm and the tops 2.25 ppm; radish roots had 0.29 ppm as against 0.80 ppm in the leafy tops.* All these contents of arsenic are below the 3.6 ppm As_2O_3 set as a safe limit for farm products in United States interstate commerce.

The danger of arsenical poisoning in orchards is not so much to the fruit trees as to the cover crop below them; the land becomes useless for growing shallow-rooted field crops. Old

* The Karroo bush, *Pentzia incana*, may deposit as much as 355 ppm of As_2O_3 in the aerial parts (Marais, Botha, and Klintworth, *Farming in South Africa*, March, 1950).

orchard soils in the Yakima Valley of Washington, which contained 4–12 ppm of soluble arsenic (calculated as As_2O_3) in the top soil, were found to have become unproductive. Alfalfa or barley germinated poorly, turned yellow, and died. Although it is possible that the lead of lead arsenate may have been a contributing factor, the soluble arsenic was found experimentally to be sufficient to account for the entire effect.[181]

The application of large amounts of calcium arsenate dust for boll-weevil control on cotton has rendered sandy loams in South Carolina unfit for not only field crops but also cotton itself. These soils were found to contain about 30 ppm of total arsenic instead of the normal 8 ppm.[1] This represents the accumulation of 50 lb/acre of calcium arsenate every year. The hazard is increased when the soil is coarse and low in humus. Cotton growing in sandy soils shows special sensitivity to arsenic poisoning; only 48 lb/acre of lead arsenate is sufficient to reduce the growth and yield, being particularly deleterious to the roots.[38] The acidity resulting from soluble arsenic in the soil may be corrected by lime; ferrous sulphate is also remedial.[36] An alternative measure is to substitute the insoluble basic copper arsenate in treating cotton on sandy soils.

Fluosilicates and fluoaluminates

The fluosilicates are more hazardous to foliage than acid lead arsenate. Although sodium fluosilicate in 0.5% suspension does not injure the young foliage of orange,[148] nevertheless when dusted on sugar cane at 16 lb/acre it causes severe scorching and a reduction in yield.[92] Solutions of sodium fluosilicate are acid and gradually hydrolyse in water to produce soluble phytotoxic compounds; neutralization with hydrated lime decreases the soluble fluorine and the phytotoxicity.[33a] Both sodium and barium fluosilicate can burn the foliage of grape at moderate doses.[145] Peach foliage is unusually susceptible to foliage and fruit injury by fluosilicates or cryolite.[115] The presence of sodium fluosilicate in soil in amounts up to 150 lb/acre is stimulating to plant growth, and no species of plants are harmed at 300 lb/acre.[114] Even at 1500 lb/acre, sodium and barium fluosilicate is harmless to those species of blue grasses that are poisoned by

an equivalent dosage of lead arsenate.[111] On the other hand, soluble fluorides are highly detrimental to plant growth.[130]

Cryolite, sodium fluoaluminate, is the safest of the fluorine compounds to use on plant foliage because of its low solubility (0.06%).[161] Orange foliage can withstand many applications of 0.15% suspensions without injury to foliage or flavour of fruit.[142] Nevertheless under cool and slow-drying weather conditions cryolite may cause injury to fruit and leaves of pomes.[9] Peach fruits may become malformed at the tip end, and sunken areas and cracks may appear.[115] Dipping the roots of tobacco seedlings in 2.5% cryolite, for control of root borers, damages up to 90% of the plants.[160] Yet natural cryolite applied to the soil in dosages up to 3000 lb/acre had no effect on the growth of lima beans or bell peppers, since the soluble fluorine is rapidly fixed by the soil.[159]

Selenium

When applied to the soil in order to protect greenhouse flowers from insect pests, selenium is absorbed to its maximum level in the plant within 3 weeks. By this time the tops of chrysanthemums, for example, contain 300 ppm of selenium in their tops, absorbed from an application of 0.5 gm/ft^2 of soil. The thresholds of phytotoxicity are 0.25 gm/ft^2 for antirrhinum, 0.5 gm/ft^2 for gladiolus, and 1.0 gm/ft^2 for carnations and chrysanthemum.[39]

Dinitro compounds

DNOC. 3,5-Dinitro-*o*-cresol is highly phytotoxic, its salts being used as weedicides. When used for grasshopper control, oil emulsions of DNOC burn wheat foliage at dosage levels of 3 lb/acre, although the grain remains unaffected; broad-leaved weeds become scorched at dosages between 5 and 10 lb/acre, some 5 times the insecticidal dose.[26] In forest insect control, the young shoots of conifers are found to be as susceptible to DNOC as deciduous leaves, but the older needles of conifers are more resistant.[31] For orchard work, the application of DNOC is restricted to dormant sprays; in trees which are leafing out, high temperatures and cool moist conditions enhance the phytotoxicity.[9] The phytotoxic effect of DNOC is characterized by acute necrosis but no chronic injury. The lethal action on plant

tissue may be due to its increasing the oxidative catabolism to a level beyond the restoring power of photosynthetic anabolism.[150] DNOC penetrates into foliage through the cuticulin of the epidermis, to which it has a staining affinity; it may also evaporate and diffuse as a gas through the stomata as well as the epidermis. It is more phytotoxic when dissolved in oil than in water, partly because the plant is not wetted by aqueous solutions. Some plants such as mustard are wetted by water, whereas the majority (such as wheat) are not; hence an aqueous solution may be used as a selective weedicide.[61] DNOC is more phytotoxic when applied as the undissociated acid, and the sodium dinitrocresylate used as a weedicide is activated by the addition of acid salts. With the unactivated sodium salt, peas and flax were able to tolerate a dose of 4 lb/acre, sweet corn 6 lb/acre, onions 8 lb/acre, alfalfa 15 lb/acre, and barley over 30 lb/acre.[184] For control of noxious weeds, from 1 to 15 gal of *Sinox* (a paste containing 30% sodium dinitrocresylate in water) is required to spray 1 acre; this is equivalent to a dose of 3 to 45 lb/acre of the dinitrocresol. DNOC is slowly decomposed in the soil to leave no toxic residue.[150]

DNCHP. This dinitro compound has been developed as a summer spray in place of DNOC, since it is much less phytotoxic and is an effective acaricide. Orchard foliage is not damaged by 0.02% suspensions, except when oil or lime-sulphur has also been applied. However, grape vines are scorched by 0.01% suspensions, which also may cause spots to appear on the flowers of some greenhouse plants.[29] When DNCHP is applied to citrus foliage in oil solution, it is harmless at 0.25% concentration, gives slight to moderate injury at 0.5%, and severe injury at 1% concentration. Injury is increased at high temperatures and low humidities. There is not sufficient margin of safety between insecticidal activity and phytotoxicity for oil solutions to be feasible, but aqueous solutions of certain organic salts have given promise. Dusts with DNCHP incorporated in an acid diluent such as walnut-shell flour are not phytotoxic to citrus, peach, or almond; but with basic diluents they are injurious to tender shoots, owing to the formation of toxic water-soluble salts.[illegible]

DNBP. The analogue dinitro-*o-sec*-butylphenol, used as a dormant insecticide, particularly in the formulation *DN-289*, is

even more destructive to plants than DNOC. It may be used safely as a dormant spray for apple, cherry, or plum if it is applied as the triethanolamine salt in 0.1% aqueous solution; but if 0.5% of oil is added, it causes light to moderate bud injury. Even the aqueous sprays are toxic to peach, severely injuring the buds and terminal twigs.[57] This dinitro compound is more toxic as a soil contaminant than DNOC, concentrations of 200 ppm inhibiting plant growth, whereas 50 ppm proves stimulating. It is decomposed by the soil microflora, so that a contamination that proved toxic to one crop may become stimulating to the next succeeding crop.

Thiocyanates

Some of the organic thiocyanates have been found to be phytotoxic, *p*-thiocyanoaniline severely injuring nasturtium.[58] However, the commercial insecticide *Lethane 410* (β-butoxy-β-thiocyanodiethyl ether) showed no foliage or blossom injury to a wide variety of plants,[131] and when applied as an acaricide in 0.25% emulsion it was entirely harmless to carnations.[132]

Azobenzene

This acaricide is generally mild to plants. However, 0.1% sprays applied to apple trees completely defoliate them, leaving only the fruit.[56] Azobenzene smokes and sprays are especially injurious to roses,[2] the flower colours fading.[164] The blossoms of violet and African violet (*Saintpaulia*) are particularly susceptible to damage by azobenzene, even in dusts which are far less phytotoxic than the smoke or fumes.

Plant derivatives

None of the insecticides of plant origin—pyrethrins, rotenone, sabadilla, ryania, or nicotine—are phytotoxic. With pyrethrins, there is evidence that the application of pyrethrum dust to potatoes results in their developing twice the normal number of blossom clusters.[113] With derris insecticides, it has been observed that the toxic principles may be translocated from dusted foliage to new undusted leaves subsequently unfolding.[66] With sabadilla dust, transient foliage symptoms have been detected on three species of squash.[illegible] Nicotine has caused wilting and ne-

crosis of potato foliage when thermally generated as a fumigant in high concentrations, presumably as a consequence of its alkalinity. The leaves of violet are particularly susceptible to damage by nicotine fumigation.

HETP and TEPP

These organic phosphates are very slightly phytotoxic. Of over 130 species of plants tested in the greenhouse, only tomato and a few varieties of chrysanthemum showed foliage injury from 10% aerosols applied at 10 gm/1000 ft^3. The injury is characterized by the appearance of black necrotic spots on the foliage, which may be surrounded by scorched areas. Roses and carnations may become susceptible to flower or leaf injury under hot or sunny conditions. But when HETP aerosols are properly applied the improvement in size and appearance is so great as to suggest stimulatory action.[161] Aerosols of HETP and TEPP may cause a transient leaf burn of many plants, among which tomatoes are most susceptible. If HETP is applied as a spray, foliage scorching appears on tomato with solutions of 0.1% strength; this, however, is far in excess of the concentration required for insecticidal effect. Tomatoes were killed when the soil was watered with solutions of TEPP in excess of 0.2%, and HETP in excess of 0.05%. When their vapours were generated thermally, HETP and TEPP "cooked" the leaf tissue, and the ethylene vapour resulting from their thermal decomposition caused an epinasty or bending of the stems similar to a plant hormone effect.[192] On orchard fruits, foliage injury has been noted on pear, peach, and plum, where it appears as red spots 1/8 in. in diameter, of which the centre drops out.[139, 157] This hazard of burning of pomes appears at high temperatures or under slow-drying conditions.[9]

Parathion

Most greenhouse and garden plants will withstand quite large doses of parathion, but tomato and cucumber are sensitive.[8] When treated with aqueous sprays containing 0.02–0.03% parathion, some 500 species of plants remained unharmed; but injury occurred to the fronds of ferns, the flower bracts of poinsettias, and the blooms of African violet, and roses responded

by dropping their leaves.[140] Roses are sensitive to leaf burning by 0.02% parathion sprays, particularly when they do not dry off quickly. Parathion in 3% dust caused transient foliage symptoms on 3 species of squash. It is safe on the foliage of orchard crops,[139] except when applied in high concentrations in cool or slow-drying conditions.[9] However, the McIntosh and Cortland varieties of apple are susceptible to precover sprays containing more than 0.01% of parathion; the young foliage shows leaf curl and develops necrotic margins, while the fruit shows necrotic spots.[8,73a,106] Epinasty of the terminal leaves has also been observed in plum foliage treated with 0.05% parathion.[95] The use of oil solutions increases the hazard of plant injury. Shrubs with light terminal buds are sensitive to injury by dormant sprays of 0.02% parathion, foliation being delayed or inhibited.[158a] It has been found that the bleaching of leaf margins is caused mainly by *p*-nitrophenol, an important impurity of technical parathion.[55a]

Parathion sprays, as well as HETP and TEPP, have been found to increase the yield of potatoes independently of their insecticidal effect; the foliage becomes greener, and remains green for a longer time. It is suggested that these phosphatic insecticides act as a nutritional factor and are absorbed through the leaves, much as an H_3PO_4 spray gives an increase in yield at levels that are not insecticidal.[186a] A concentration of 200 ppm of parathion in the soil was not only non-toxic to corn but appeared to be somewhat beneficial. Two weeks after its application, the leaves of the corn plants were insecticidal to *Pyrausta* larvae.[143] When soil was treated with 600 ppm of parathion 1–10 days before seeding, the growing plants were protected against aphid attack. Potatoes were protected against *Macrosiphum* from the third to the eighth week after planting, and nasturtiums were protected against *A. rumicis* until the seventh week. The protection of squash from *A. gossypii* was less effective, and beans were not protected against the two-spotted mite. This concentration of parathion caused a very slight reduction in the growth rate of the plants.[77]

The data reported above have not been accepted as conclusive evidence of translocation from root or seed, since the parathion in the soil may have had a fumigant effect in the aerial parts above it.[3a] Indeed, parathion is not translocated from the

sprayed foliage to the developing fruit except in the minutest quantities.[163a]

The new acaricide EPN has failed to cause noticeable fruit or foliage injury, except to McIntosh apples, when applied at the recommended dosages.

Systemic insecticides

These compounds, being either organic phosphates or fluorohydrins, exhibit the property of being taken up into the plant and translocated to the leaves, presumably as intact molecules, sufficiently to exert insecticidal action on phytophagous insects. Bis(bisdimethylaminophosphonous) anhydride is the least phytotoxic of these compounds hitherto tested.[19] It is harmless to brussels sprouts, sugar beets, and hops even at high concentrations. At moderate concentrations peas develop necrotic spots, and at light concentrations (0.05% and over) broad beans develop necrotic areas on the leaves 3 weeks after application. Potatoes are susceptible under certain conditions, and certain varieties of apple may show defoliation and fruit drop.[149] This insecticide (OMPA) is not sufficiently harmless to be used in hydroponics.[19]

The bis(dimethylamino)fluorophosphine oxide is much more phytotoxic. The fluorohydrins bis(2-fluoroethoxy) methane and bis(2-fluoroethyl) ether are of intermediate toxicity.[19, 53]

The tetrakis anhydride has been reported to be more powerfully systemic than the fluorophosphine oxide by Schrader, but to be weaker by Martin. It is translocated to the growing parts of the plant when applied to the roots, cut stems, cuticle, or stomata of leaves, which become aphicidal when they contain 100 mg/kg of the insecticide.[43a] Naturally the systemic effect no longer obtains when the plants have stopped growing.[149] Whereas when the material is applied to the roots it is translocated everywhere in the plant, when applied to the upper surface of the leaf it is translocated only to the undersurface, and undersurface applications are not translocated anywhere in broad beans.[44] Upon repeated treatment, the material is translocated from leaf to leaf, although the broad bean shows less translocating activity than other plants.[43a]

DMC and DCPM

These two chlorinated acaricides have been described as characteristically non-toxic to plants. DMC in the form of a 25% miscible concentrate diluted 1:800 in water has caused no foliage, flower, or fruit injury to orchard trees or to greenhouse plants. At higher concentrations, slight injury to foliage of peach and grapes and to flowers of *Antirrhinum* and *Saintpaulia* may occur, and Boston and asparagus ferns may be killed at a dilution of 1:200.

With DCPM used in the recommended 0.05% suspensions, no injury has been detected on the foliage or fruit of orchard trees, with the exception of a slight increase in a russetting which occurred from other causes in certain districts. However, certain succulent plants such as beans and tomatoes have suffered a stunting of the foliage.

Toxaphene

This chlorinated camphene is generally safe for application to plant foliage, except in certain cases. Toxaphene in 0.4% suspensions was found to be harmless to 70 species of trees and shrubs, the only exceptions being sugar maple and the Imperial Gage variety of plum.[169] It does not cause injury to apple foliage except when used with oil. Although harmless to most pears, toxaphene russets the fruit of the Comice variety, and may burn foliage if used with oil.[31] It is phytotoxic to peach foliage, causing chlorosis and marginal burning; wettable sulphur, however, may act as a safener.[162] Potatoes appear to be rather susceptible, 0.1% toxaphene suspensions causing slight injury,[180] and chlorosis being induced by 0.4% suspension sprays.[136] The 0.1% suspensions severely stunt and sometimes kill cucumber and cantaloupe, although they are harmless to lima beans or grape foliage. Toxaphene in 2.5% dusts can severely injure squash and other cucurbits; injury is greater at high humidity and with young plants.[170] Italian prune also has been injured, and young corn is damaged by toxaphene in oil solution.[187] A 3% dust made from technical grade toxaphene killed all plants of *Cucurbita pepo* (table queen squash), and a quarter of the *C. moschata* (butternut squash) plants to which it was applied.[33]

Toxaphene is the only chlorinated hydrocarbon insecticide that is detoxified in the soil at an appreciable speed.[13] When incorporated in the soil at 25 lb acre it did not injure any crop plants.[129] However, at low concentrations it may depress seedling growth.[42]

Chlordane

Technical chlordane, which is a mixture of chlorinated hexahydroindenes, offers less foliage hazard than chlorinated camphene; it is, however, more hazardous as a soil contaminant. Chlordane is not toxic to apple foliage,[9] although it has injured spring foliage of plum and cherry.[86] A 0.1% suspension has caused severe defoliation, some bud injury, and slight fruit damage to plum.[95] Three species of squash showed only transient symptoms when treated with a 3% dust of chlordane.[33] When used in greenhouses it has caused leaf fall of *Abutilon* and injury to *Poinsettia*.[7] Chlordane sprays may burn the foliage of tomato transplants; the foliage hazard is enhanced by dew.[103]

Chlordane is stable in the soil and is fungicidal.[13] At 10 lb acre it had no effect on cereals, vegetables (including soybeans), annual flowers, or grasses.[62] At low concentrations, however, chlordane may depress seedling growth without inducing any pathological symptoms.[42] At 25 lb acre, none of the plants grown in the soil showed injury except lima beans, which were slightly stunted and chlorotic.[129] However, chlordane may severely affect the germination of some seeds at this dosage.[13] At 50 lb/acre, the germination of tobacco is destroyed, but that of cabbage, lettuce, and tomato is unaffected.[103] Chlordane does not become destructive to turf until dosages exceed 100 lb acre, at which level clover and bent grass become susceptible.[158] Soil applications of aldrin at 100 lb/acre do not injure or inhibit the growth of field crops.[101a]

BHC

Benzene hexachloride is perfectly safe for orchard work in cases where it is used for aphid control.[157] But if used in wettable powders or dusts which contain more than 0.04% of the gamma isomer (lindane), it will be found to scorch or damage the seedlings of radish, turnip, kale, spinach, and beet root.[171]

BHC smokes, like azobenzene, are particularly injurious to roses. Dusts containing 3% BHC applied at 30 lb/acre seriously affected the foliage and yield of two species of squash, *Cucurbita pepo* and *C. moschata*, and moderately injured the foliage of *C. maxima* (Blue Hubbard squash).[33] Dusts containing 3% BHC applied at 30 lb/acre scorched the foliage of cucumber and cantaloupe, severely injuring the new growth; 1% BHC (1/3 gamma) dusted at 175 lb/acre injured sweet corn, but not lima beans.[25] Suspensions of 0.1% BHC (12% gamma) injured the foliage of tobacco seedlings.[50] Lindane is not the phytotoxic principle of BHC. Preparations of BHC that contain over 90% of the gamma isomer (e.g. *Hi-Gam*) are not phytotoxic to foliage of cucurbits that are susceptible to the usual grades of BHC.[10,152] When the individual isomers are tested, only the delta isomer is found to be toxic to leaf and stem.[152]

However, the most important hazard involved in the application of BHC to plants is the tainting of their flavour with a characteristically musty odour and taste. Suspension sprays containing 1% BHC (1/9 gamma) taint the flavour of potatoes, peas, carrots, beet root, marrows, cauliflower, and lettuce, and some crops may be tainted by 0.1% suspensions.[174] The taint enters the pea in the pod even if application is made no later than blossom fall.[183] Orchard fruits may escape the taint if applications are confined to the first cover sprays; but if these peaches, apples, pears, or cherries are cooked or canned, the taint will appear.[141] Where BHC has entered the soil, it unavoidably taints root crops such as potatoes, although onions and radish may be unaffected. A soil dosage of 5 lb/acre BHC (1/8 gamma) is sufficient to taint potatoes, but fortunately it may lose this property after 2 or 3 years.[11] The aerial parts of plants are not so susceptible to tainting *via* the soil, but peas and pole beans are more susceptible to this BHC hazard than the majority of crops.[173] It has been shown that BHC is translocated in the potato into the foliage and tubers.[168a] Again it is found that lindane is not the tainting principle of BHC. The odorous and odious material is considered by some to be derived, possibly as a breakdown product, from the beta isomer. At any rate, samples of purified lindane are declared by most observers to be practically odourless.[10] Commercial samples of lindane or high-

gamma BHC are far less tainting to crops than commercial BHC.[10,141] When the individual isomers are compared, the beta and delta are found to taint more frequently and strongly than the alpha and gamma isomers.[152]

When BHC applications accumulate in the soil, they persist for a long time. As much as 80% remains intact after a period of 18 months in fine sandy loam, whether acid or alkaline; while 95% of added DDT remained unchanged.[167] Indeed, as judged by its toxic effect on *Anomala*, BHC in Hawaiian soils disappeared even more slowly than DDT.[156] Benzene hexachloride has no effect on the *p*H of the soil or on its bacterial content. *Azotobacter* and other bacteria, *Actinomyces* and other fungi, are unaffected, although the delta isomer is highly toxic to algae.[186] Soil containing 100 lb/acre of BHC (10% gamma) proved harmless to any crop plants grown in it. Soil containing 275 lb/acre of this BHC did not affect broccoli, cabbage, carrots, celery, mustard, parsnips, and radish, and indeed stimulated the vigour of the cruciferous plants; but it adversely affected lettuce and pepper, stunted beans and tomatoes, and killed beets, cantaloupe, chard, corn, cucumber, onion, peas, potatoes, pumpkin, spinach, squash, and watermelon.[129] BHC (30% gamma) at 100 lb/acre in the soil injured sweet corn, peanuts, cotton, and soybeans.[80] At 60 lb/acre, BHC of 30% gamma content caused severe root injury to garden peas, although the expected decrease in germination rate did not occur until the dosage was higher.[156] The growth of legumes is reduced in soil containing more than 30 ppm of regular commercial BHC.[186] Onions are not affected until the concentration of BHC exceeds 200 ppm (0.5 gm/2 lb of soil), when the root tips are turned brown and the roots become shorter and thicker, till at 800 ppm no seedlings emerge above ground.[125] At concentrations of BHC (10% gamma) in excess of 200 ppm, the roots of wheat, flax, cabbage, beet, and cress develop brown patches, lack root hairs, and fail to strike down into the soil; oats are so susceptible that they show this effect at a 25-ppm level of BHC.[167] Rye is the least susceptible of the cereals to damage by lindane.

It has been concluded that although BHC reduces the percentage emergence of seedlings from the ground, it does not affect germination. The fundamental effect of commercial BHC on

germinated seed and growing seedlings is to induce ploidy of the chromosomes in root, stem, and coleoptile, an effect similar to that of colchicine. The result is enlargement of the cells, the epidermal cells becoming large blisters, and the root tip and coleoptile being shortened and thickened; the germination of brassicaceous plants is stimulated.[108] There is evidence that the factor in BHC which reduces germination, and which causes necrosis of root tips and the lack of root hairs in wheat seedlings, is a breakdown product and possibly one of the trichlorobenzenes.[200] It has been found that the vapour of 1,3,5-trichlorobenzene deforms germinating wheat seedlings.[67]

DDT

High-grade commercial DDT has been found to be completely harmless to the foliage of a wide variety of plants and their seedlings, when applied as a suspension or oil-free emulsion. Instances of phytotoxicity, which have occurred with elm and which are a regular occurrence in plants of the Cucurbitaceae, may be referred either to the detergent in the wettable powder formulation, or to impurities in the commercial grade of DDT. The application of 10% DDT dusts is harmless to all kinds of crops, including cucumbers; only crookneck squash was injured.[42] Aerosols applied to greenhouse plants at the rate of 5 mg/1000 ft^3 of DDT were harmless to all species except cucumber, whose leaves developed slight etiolation and chlorosis, but this could be remedied by substituting methylnaphthalene for cyclohexanone as the solvent.[164] Suspensions containing 2 lb/100 gal of a 50% wettable powder induced foliage chlorosis of varying degrees in 24 varieties of squash, 11 of muskmelon, and 7 of watermelon.[27] Kalanchoes are consistently injured by DDT dusts, sprays, or aerosols, the aerial parts suffering epinasty and chlorosis until most of the plants above ground have been killed.[112] Certain varieties of squash are more susceptible than others. Those derived from *Cucurbita pepo* (table queen, yellow summer, acorn, etc.) are invariably yellowed, scorched, and killed when treated with 1 lb/acre of DDT in the form of a dust. With *C. moschata* (e.g. butternut), only half of the plants died; with *C. maxima* (Hubbard, buttercup), none of the plants died, necrosis did not occur, and the chlorosis was transient.[42] If a high-grade DDT

(setting point 104° C) was substituted for the commercial DDT (setting point 90° C) in the dusts, no phytotoxicity was shown to any of the varieties.[33] It is therefore probable that the epinasty, chlorosis, and necrosis are due to the impurities in the technical product, although it is possible that the stunting and interveinal yellowing of cucumber and marrow are due to DDT itself.[174] The restoration of the sulphone impurities of technical DDT to purified DDT results in reappearance of its phytotoxicity.[42] Technical DDT applied as wettable powder to orchard trees may cause foliage and fruit injury at high temperatures and humidities.[9] The foliage of American or Chinese elm has been scorched, has developed chlorotic spotting, or has been partially or completely removed from the tree, by 0.3–0.4% suspensions or 0.2% emulsions.[45, 153] It is possible that the causative agent may have been the emulsifier or detergent. The foliage of tobacco seedlings is injured by DDT suspensions when used at concentrations higher than 4 lb/100 gal.[50]

Whereas DDT applied as dusts or wettable powders in normal practice is not absorbed into the tissues of crop plants, when in oil solution it penetrates into the rind of citrus fruits.[34] Olive fruits can absorb DDT from suspension deposits,[168] presumably because of their own oily nature. When DDT is deposited on tropical foliage, it is absorbed and translocated both below and above the point of application, and appears in stem and root.[17] Little residual toxicity is therefore left on the surface of the leaves; this effect is much more marked with hairy leaves than with glabrous, and the former types are susceptible to scorching by the oil.[176a] DDT may be artificially translocated into terminal foliage of bean by applying DDT-lanolin pellets or by wicks carrying DDT suspensions.[96] A 5% solution of DDT in kerosene causes cocoa pods to blacken rapidly and be attacked by fungi, an effect not produced by solvent or solute alone.[75] Squash plants have been killed outright and papaya (*Carica*) severely injured by oil solutions of DDT applied from aircraft for mosquito control.[16] Emulsions of DDT containing 0.3% white oil induce a chlorotic mottling of pear foliage.[171] Even on apple foliage, the addition of summer oil to DDT suspensions was found to induce foliage injury.[21] When applied to the foliage of citrus trees in 3% kerosene emulsion, DDT may im-

mediately penetrate into the leaf, to creep out to the surface again, so that the surface deposit 1 day later is greater than that a few minutes after application.[81]

DDT is highly persistent in the soil, only 5% being lost in 18 months.[167] At 20 lb/acre it still kills wireworms after 5 years.[183] It has no effect on soil pH or bacterial content.[167] Even at 5000 ppm, there is no effect on ammonifying or nitrifying bacteria, and at 20,000 ppm DDT is harmless to legume nodulation and their bacteria.[185] Repeated cropping does not change the picture given by a DDT-treated soil.[129] It is not toxic to fungi, as shown by tests on 6 species;[185] certain wood-rotting fungi can grow in 3% DDT solutions.[123] In fact, it promotes the development of damping-off organisms.[42] However, the application of DDT dusts to potato foliage appeared to have a considerable fungicidal value. And it was observed that the wheat variety Khapli became resistant to rust (*Puccinia*) after being sprayed with DDT.[99]

When commercial DDT was added to the soil at the rate of 25 lb/acre, only lobelia, alyssum, gaillardia, scabious, and strawberry were affected out of 270 species of ornamental plants and grasses; of 21 crop species, including 3 cucurbits, only beans, tomatoes, spinach, soybeans, and onions were affected; in all cases the effect was retardation of growth.[61] At 140 lb/acre, bush and pole beans were severely stunted, as well as tomato transplants.[129] At 200 lb/acre, the yield of beans (Black Valentine) was reduced by 57%, and of rye (Abruzzi) by 33%.[42] Yet when purefied DDT is used, neither bush or lima beans, nor tomatoes, are affected at 200 lb/acre.[61] With impure DDT, a concentration of 430 ppm severely stunts tomatoes and beans;[129] with pure DDT, the growth and germination of all species tested were normal at 20,000 ppm.[167] Bean and carrot seed treated with commercial DDT was delayed in its germination, but its growth was unimpaired.[128] Seeds planted in sawdust containing impure DDT were delayed in germination but accelerated in growth.[illegible] Legumes grown in sand were reduced in height when 100 lb/acre of technical DDT was added, and root nodulation was decreased at 1000 lb/acre of DDT.[11] The toxicity of DDT in the soil is reduced as the content of organic matter is increased. The ap-

plication of lime to some soils markedly increases its toxicity. Conversely the toxicity is reduced as the soil acidity is increased, except in the case of rye.[43]

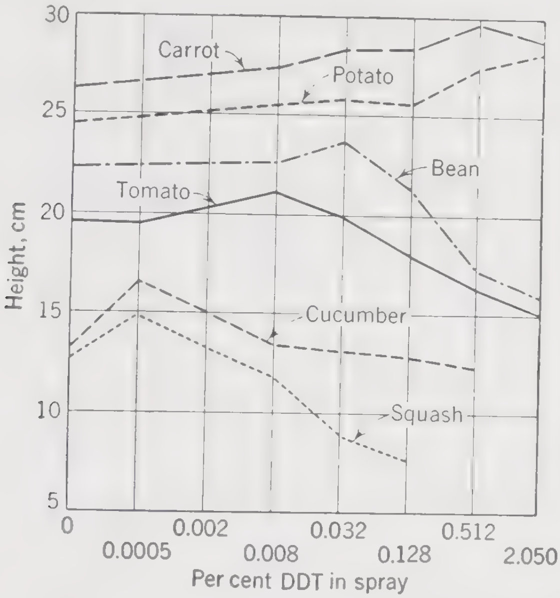

FIG. 3. Effect of DDT sprays on growth of certain crop plants. (From Chapman and Allen)

Commercial DDT also causes stimulation of growth. At 430 ppm in the soil it increases the vigour of cabbage and lettuce seedlings, an effect independent of the microflora.[129] When a low concentration of impure DDT (setting point 89° C) is applied as a suspension to any part of a plant, including the roots, a stimulation of its growth in height (Fig. 3) and number of blooms results.[45] The foliage generally becomes a brighter green, and there is an overall increase in weight up to a maximum of about 20%. There is an optimum concentration for this effect, depending on the sensitivity of the plant, as follows: squash and cucumber, 0.0005%; tomato, 0.008%; bean, 0.032%; carrot and potato, 0.5% or more. As the concentration is increased above this level, stunting, deformity, chlorosis, and necrosis progressively appear. Thus the most susceptible species to injury are the cucurbits, and the most resistant are carrots and potatoes, as also peas and corn, which are not stimulated by light doses. This stimulation resembles the sublethal effects of 2,4-D and

other plant hormones; how far it is due to impurities it is at present impossible to say.

There is little information available on the phytotoxicity of the analogues of DDT, such as DDD, DFDT, and methoxychlor, apart from the fact that they are harmless to most plants. DFDT has been found to be slightly phytotoxic to sweet corn. Methoxychlor dusts applied to squash foliage engender in their surface a transient rugosity that is reminiscent of grained leather. However, it has been concluded that methoxychlor is the least injurious, to cucurbits, of the chlorinated hydrocarbons, all of which may cause damage under moist conditions.[41a]

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CHAPTER IX

Chemical Control of Insects Feeding on Plants

General considerations

The chemical control of phytophagous insects was revolutionized by the appearance of DDT in the 1940's. This material as commercially prepared is almost completely safe for the foliage of plants, with the exception of cucurbits. It does not taint the plant juices, nor are its deposits unsightly. DDT may persist on the foliage for over a month, since neither heat nor light destroys it, rain does not dissolve it, and it is lost by evaporation very slowly. If heavy applications are avoided shortly before harvest, the DDT residues on the crop are not sufficient to involve hazard to the consumer. However, when used as feed for dairy cattle, it is secreted in their milk, which forms a staple in the diet of young human beings; therefore the use of DDT on forage crops is prohibited. Its place may be taken by the other chlorinated hydrocarbons which are not secreted in milk, or by ryania, sabadilla, or pyrenones, depending on the crop.

The place which DDT has won in the control programme for the various phytophagous insects has been summarized by West and Campbell.[133] In this chapter, references previous to 1946 will be ascribed to them rather than to the original workers, who may be located from their book. The literature up to 1949 shows

that the insect groups for which DDT is the most practically effective insecticide are:

> Mirids, tingids, membracids, cicadellids, thysanopterans, pierids, lasiocampids, geometrids, tenthredinids, cerambycids, buprestids, bruchids.

There are many large and important groups for which DDT is the best insecticide except for one or two aberrant species. They are as follows, the exceptional species and the substitute insecticide being cited:

Sphingids	*Protoparce sexta*	Pb arsenate, basic Cu arsenate
Arctiids	*Estigmene acraea*	Toxaphene
Phalaenids	*Alabama argillacea*	Ca arsenate, toxaphene
Tortricids	*Argyrotaenia* spp.	DDD, parathion
Pyralids	*Diatraea saccharalis*	Toxaphene, cryolite
Chrysomelids	*Crioceris 12-punctata*	Chlordane, toxaphene
Scolytids	Ambrosia beetles	BHC

There are a number of groups for which DDT is an effective insecticide, but other materials are practically superior. They are as follows:

Curculionids	Chlordane, toxaphene, BHC
Cutworms	Chlordane in baits
Cercopids	Chlordane
Tenthredinid leaf miners	Nicotine
Agromyzid leaf miners	Chlordane
Fruit flies	Parathion

Finally there are the groups for which DDT is inferior or ineffective; they are composed mainly of the heavily sclerotized forms, soil insects, and those with a very rapid life cycle:

Orthoptera	Chlordane, aldrin, parathion, BHC, toxaphene, DNOC
Larger Hemiptera	BHC, parathion, chlordane
Cicadid adults	TEPP
Psyllids and aleyrodids	Parathion, TEPP, rotenone, nicotine
Aphids	Parathion, TEPP, BHC, nicotine
Coccids	Parathion, dinitro compounds, oils, HCN
Psychids	Toxaphene, lead arsenate

Hymenoptera (adult)	BHC, parathion
Anthomyiids (root maggots)	Calomel, BHC
Elaterids (wireworms)	BHC, aldrin, parathion
Epilachna varivestris	Parathion, pyrethrins, rotenone
Scarabaeids (white grubs)	BHC, aldrin, parathion
Lyctids	Pentachlorophenol
Anthonomus grandis	Toxaphene, BHC
Conotrachelus nenuphar	Chlordane, BHC
Acarina	DNCHP, DMC, DCPM, TEPP, parathion, etc.

These groups are composed of the heavily sclerotized forms, such as Orthoptera, the larger Hemiptera, Cicadidae, Hymenoptera, *Epilachna*, *Anthonomus*, and *Conotrachelus*, on which DDT cannot exert its characteristic contact action; or of insects with a very rapid life cycle, such as aphids, psyllids, coccids, or Acarina; or of soil insects, such as root maggots, wireworms, and white grubs, where DDT lacks the fumigant action necessary for a soil insecticide that is to be effective at low concentrations.

The volatility of an insecticide is very important in deciding its insecticidal characteristics. Chlordane, lindane, and parathion have shown themselves to be highly toxic low-vapour-pressure fumigants. Toxaphene and DDD have inferior fumigant properties, while DDT has none at all. The role of volatility in deciding effectiveness is best exemplified by the differences in susceptibility of *Myzus persicae* on crops of various foliage types (see below). On the flat laminate leaves of peach and tomato, it is adequately controlled by DDT, since there are no crevices where the aphids can escape its contact action. On cabbage, with the deep interleaf recesses, DDT is effective only after repeated applications. On celery, with its wrinkled upper foliage, DDT is markedly inferior to TEPP and parathion. For *Myzus* infesting the excessively convoluted foliage of spinach, an insecticide possessing fumigant action (such as BHC) is required to penetrate all the crevices.

Volatility also decides the duration of effectiveness after the initial application. It is well known that the field performance of BHC is disappointing, as compared with its outstanding toxicity in the laboratory, because it soon volatilizes from the crop; chlordane partakes of this characteristic to some extent. On the

other hand toxaphene, although less toxic than chlordane, gains as a residual insecticide because it approaches DDT in its resistance to evaporation.

The liability to taint the crop puts a severe limitation on the use of BHC in its present commercial forms. Even chlordane can taint some crops such as corn. Its phytotoxicity also puts BHC at a disadvantage; in a few cases (e.g. peach) this applies also to chlordane and toxaphene.

The instability of TEPP gives it a notable advantage in allowing applications to be made close to the time of harvest. As with nicotine, the deposits rapidly disappear and leave no hazardous residue. Parathion, at the extremely low concentrations adequate for insect control, volatilizes fast enough to leave no residue hazard if applications are ceased a month before harvest. Certain of the organic phosphates and fluorohydrins exhibit the property of being absorbed and translocated in the plant, and are employed as "systemic insecticides" for aphid control, the plants being rendered insecticidal and remaining so for some weeks.

Non-volatile and highly persistent insecticides leave residues which involve a hazard not only to the consumer but also to the beneficial insects inhabiting the crop. DDT is an even worse offender than the arsenates, its use often being followed by outbreaks of aphids, coccids, and certain tortricids; these are due to the destruction of the parasite and predator population by the DDT, while the insect pest itself has been only partially controlled. The shortcomings of DDT in penetrating leafy shelters to reach certain tortricids such as *Argyrotaenia velutinana* and *A. citrana* may be remedied by the substitution of DDD; the same applies to the control of *Heliothis armigera* within the ears of corn, where DDD again proves more effective than DDT.

The most serious disadvantage of DDT resides in its lack of ovicidal action for Acarina, when combined with its lethality to the mite predators. For that reason the application of this insecticide has been followed by infestations of tetranychid mites, particularly in orchards where this material may be applied at intervals throughout the entire summer. The eminent suitability of DDT for codling-moth control has demanded the development

of an entirely new field of mite ovicides to correct its shortcomings in that direction.

However, modern research is moving towards the development of highly insecticidal, penetrating, ovicidal, non-phytotoxic, and non-persistent compounds that are effective in extremely low concentrations. The danger is that such highly toxic substances may involve a serious hazard to the men making the application. Parathion is an example, for it can destroy almost every species of insect and acarine in all its stages; already it has claimed its human victims among plant workers and spraymen.

In the following pages, the formulation of wettable powder sprays will be quoted in the shortest possible way: for instance, a spray composed of 2 lb of 50% DDT wettable powder per 100 gal (whether imperial or U. S.) will be described simply as a 0.1% DDT suspension.

Orthoptera

Grasshoppers and other orthopterans, with the exception of those species that have the habit of swarming, are most thoroughly controlled by poisoned baits. Since these baits are broadcast over the surface of the ground, the most suitable carriers are wheat bran, rolled oats, and chopped cereal (oats, maize, etc.); they may be diluted with sawdust. The earliest poison to be used was Paris green, followed later by arsenious oxide and sodium arsenite. The latter arsenical was extensively employed in the 1930's against *Melanoplus mexicanus*, *M. bivittatus*, and *Camnula pellucida* on the Canadian prairies, against *Melanoplus differentialis* and the Mormon cricket (*Nemobius fasciatus*) in the western United States, and against the Moroccan locust (*Dociostaurus*) in Transcaucasia. Zinc phosphide baits were broadcast against mole crickets (*Gryllotalpa*) in Egypt. Still later, sodium and barium fluosilicates came into use, the latter against mole crickets (*Scapteriscus*) in Florida, the West Indies, and Egypt, and the former against *Nemobius* and *Melanoplus* spp. in the United States and Canada. The fluosilicates were safer to use than zinc phosphide[252] or arsenicals and were no less effective as insecticides.

Locusts appearing in swarms have been attacked by applying sodium arsenite dusts from aircraft; these species include the

migratory locust (*Locusta migratoria*) in Russia, and the red locust (*Nomadacris septemfasciata*) and brown locust (*L. pardalina*) in South Africa.[314] Shortly before World War II, the organic chemical DNOC proved superior and safer for use in dusts against the brown locust in South Africa, and at the end of the war DNOC dusts were used against the desert locust (*Schistocerca gregaria*) in Persia[196] and *S. paranensis* in Argentina. DNOC sprays in oil solution were much more effective than dusts for aircraft application, dosages of 2 lb/acre giving complete kill of the red locust in Tanganyika.[197] In Alberta all adult *M. mexicanus* were killed where the deposit on the ground exceeded 0.5 lb/acre of DNOC.[68] In Saskatchewan similar results were obtained with DNOC emulsions applied from the air against *Camnula* nymphs.[64]

At the end of the war the chlorinated hydrocarbon insecticides became available. DDT proved relatively ineffective as a contact poison to *M. femur-rubrum*,[426] *M. mexicanus*,[67] and *L. migratoria*. But it has proved as toxic as sodium arsenite in baits for the migratory locust,[139] and "residual sprays" of DDT contributed to the control of *Dichroplus* spp. in Chile.[150] BHC (10% gamma content) proved to be inferior to DNOC in sprays against *M. mexicanus* and *Nomadacris*[197] and in dusts against *L. migratoria*. Technical chlordane was discovered to be twice as toxic as DNOC by direct contact, and exhibited a high residual and stomach toxicity which was lacking with DNOC.[67] The effectiveness of chlordane is materially reduced when it is used as a dust; chlordane dusts proved inferior to BHC dusts against *Melanoplus* spp. in Illinois[428] and Oklahoma,[57] although they remained considerably superior against *Chortoicetes* in Australia[10] and *Melanoplus* in Colorado.[273] Since the effectiveness of BHC dusts is enhanced by a higher temperature,[57] it is probable that the discrepancies may be related to the weather obtaining at the time of application. The control obtained with BHC dusts against *Melanoplus* spp., on the basis of the deposit of gamma isomer, ranges from 95% at 0.5 lb/acre in Oklahoma,[57] 98% at 0.5 lb/acre in Nebraska,[221] and 98% at 2.5 lb/acre in Colorado,[273] to 100% at 0.3 lb/acre in Illinois.[428] BHC is effective in sprays, 0.1% suspensions of the 12% gamma product giving

100% kill of *Melanoplus* spp. attacking orchards in Maryland, where the usual DDT and lead arsenate orchard sprays had proved ineffective.[186]

Toxaphene is another effective poison for grasshoppers. Although its toxicity rating as the result of laboratory tests is very much lower than chlordane,[426, 427] in field applications it is not very greatly inferior. When applied as sprays at 2 lb/acre of toxicant, toxaphene gives 95% kill as against 98% with chlordane.[273] Similar degrees of control are given by the spraying of toxaphene at 1.5 lb/acre and by chlordane at 1 lb/acre, or by the dusting of toxaphene at 2 lb/acre and by chlordane at 1.5 lb/acre.[322] When sprayed as wettable powders, the dosage recommended is 0.75 lb/acre of chlordane or 1.5 lb/acre of toxaphene; this is more effective where there is sufficient vegetation for the grasshoppers to eat; with young nymphs the dosage may be reduced to 0.5 and 1 lb/acre, respectively.[211, 344] Where the vegetation is sparse, DNOC at 1 lb/acre and lindane at 0.25 lb/acre may be equally effective. The low-pressure boom sprayers used for weedicides, or turbine spray blowers, are the most efficient applicators for grasshopper control, fog applicators being unreliable in attaining the necessary degree of deposition.[344] In farm practice, trap strips of vegetation may be left undisturbed and later poisoned.[31] Parathion has proved to be very much more toxic to grasshoppers than chlordane.[427] Dusts containing 2% of this material applied at 10 lb/acre have given excellent control, comparing favorably with 3% or 5% lindane dusts, or 10% chlordane or toxaphene. Both parathion and lindane kill fast by direct contact and possibly fumigant action, a higher temperature increasing the effect; chlordane and toxaphene kill slowly, acting largely as stomach poisons.[57, 167] Poisons approaching parathion in toxicity have been found among the chlorinated terpenes in the form of heptachlor, aldrin, and dieldrin (Table 1), and these derivatives are outstandingly effective when applied at 2–4 oz/acre.[127] Aldrin has established itself as the best insecticide for grasshopper control on the Canadian prairies; and its use is recommended in the United States at 2 oz/acre in emulsion or 3 oz/acre in dust form.[314a] Dieldrin is effective in Canada at the amazingly low rate of 1 oz/acre.

TABLE 1. POISONS FOR THE GRASSHOPPER *Melanoplus differentialis*[427]

LD_{50}, μg/gm of body weight

	Contact	Stomach
Toxaphene	61.0	91.5
Chlordane	9.8	12.0
Lindane	3.4	6.7
Heptachlor	1.6	4.4
Aldrin	1.8	2.3
Dieldrin	1.4	3.7
Parathion	0.8	8.9

The chlorinated hydrocarbon insecticides have been used with success in broadcast baits. BHC baits have been tested against *S. gregaria* in Kenya and Algeria and against *Chortoicetes* in New South Wales. When applied as 4% baits at approximately 5 lb/acre against *M. mexicanus* in Alberta, BHC gave 60% control as against 80% with chlordane, 70% with toxaphene, and 40% with sodium fluosilicate. Complete control was achieved with 4% chlordane baits at 15 lb/acre.[65] For the control of *Melanoplus* spp. with "dry" baits (consisting of bran "moistened" by 5% of a refined white oil containing the insecticide) application at 5 lb/acre is recommended, using 1% toxaphene or 0.5% chlordane. Wet baits, where the bran-insecticide mixture is moistened with an equal weight of water, are applied at 20 lb/acre; at this dosage, a poison content of 0.5% chlordane proves to be as effective as 6% sodium fluosilicate. Baits not only are economical to apply, but also give better control than sprays or dusts, particularly in dense vegetation.[322] However, there is a danger that certain species of grasshoppers will consume more bait than is necessary for a lethal dose (300 times as much) and leave no bait for their successors in high populations.[321a] For Canadian conditions, the content of poisons necessary for effectiveness in baits broadcast at 20 lb/acre is 4% fluosilicate, 1% chlordane or toxaphene, and 0.25% lindane.

Chlordane has been used with success for the control of mole crickets (*Scapteriscus acletus* and *vicinus*) in Florida, either as sprays containing 0.02 chlordane applied to the soil at 100 gal/acre, or bran baits containing 2% chlordane broadcast at 50 lb/acre.[254]

The larger Hemiptera

The pentatomids have proved to be comparatively resistant to chemical control, being immune to stomach insecticides and demanding strong contact insecticides. Perhaps this is a fortunate circumstance since so high a proportion of the species are predators. The harlequin bug (*Murgantia histrionica*) was formerly controlled only if completely covered with oils or oil emulsions, thiocyanates, or strong soap solutions.[291] The nymphs are able to survive DDT aerosols; but 10% dusts can kill the adults,[433] and 20% DDT dusts can give complete crop protection against all feeding stages of this insect.[151] Derris dusts can also kill the adults. The southern green stinkbug (*Nezara viridula*) requires a concentration of 10% DDT in dusts for complete control.[214] In Australia, however, *Nezara* has been controlled both by 1% dusts and 0.1% sprays of DDT.[388] Toxaphene, BHC, and parathion are equal or superior to DDT, derris is slightly inferior, and chlordane or sabadilla is ineffective.[166]

The Say stinkbug (*Chlorochroa sayi*) is readily killed by dusts of DNOC or DNCHP, but it is very slowly affected by DDT even in 10% dusts. With *C. ligata*, a 2% DDT dust killed 66% and a 5% dust killed 80% of the adults.[433] For the grain bug (*C. uhleri*) of Alberta, DDT had little insecticidal activity; moderate toxicity was shown by HETP and chlordane as well as DNOC and DNCHP, and pyrethrins and lindane were highly toxic. The green bug (*Toxoptera graminum*) that attacks oats has been found to be resistant to dusts containing 5% DDT or 1% rotenone, and it recovered its numbers after decimation by 3% HETP; dusts containing fully 3% lindane were required, 2% being inadequate.[110] The pentatomid *Biprorulus* on citrus in Queensland required 0.2% DDT suspensions to control, the 0.1% strength being deficient in residual action.[283] The genus *Euschistus* is more susceptible, *E. tristigmus* being controlled by 0.1% DDT sprays and *E. impictiventris* by 2% DDT dusts.[1[illegible]] Sabadilla is also very effective against *E. tristigmus*, a major cause of cat-facing on peaches; it is followed by BHC, toxaphene, and chlordane.[440]

The squash bug (*Anasa tristis*) is comparatively resistant to chemical control. Concentrated pyrethrin sprays and dusts will

control it,[291] and sabadilla dust is even more effective.[411] Although it has been controlled by DDT dusts from 1 to 10% concentration, wettable powders and dusts below 5% concentration have on occasion given negligible control.[19, 291] Both BHC and chlordane are more toxic than DDT to the squash bug.[421] DDT dusts or suspensions were found to give inadequate control of the leaf-footed bug (*Leptoglossus phyllopus*) on potatoes.[19] The milkweed bug (*Oncopeltus fasciatus*) is resistant to contact poisoning by DDT, but very susceptible to DNOC, DNCHP, or BHC.[69] The lygaeid *Nysius vinitor*, infesting potatoes in Australia, could be completely eradicated with dusts containing not less than 2% DDT, the 1% dusts being ineffective.[274]

The chinch bug (*Blissus leucopterus*) has been controlled by guarding fields with barriers of creosote to repel,[291] and later with sabadilla to kill,[411] the invading nymphs. DNOC and DNCHP were even more effective barriers since they killed quickly; on the other hand DDT killed much more slowly.[19] Nevertheless, 5% DDT has been found to constitute as effective a barrier as 8% DNOC dust, and it may also be used with success in area control.[433] Chlordane is more toxic than DDT to *Blissus* in turf, and aldrin is twice as toxic as chlordane.[372] Both *Blissus hirtus* and *Anasa tristis* are readily controlled by benzene hexachloride.[315] Ryania may be profitably used for chinch-bug control in small grains.[43]

Mirid plant bugs

Infestations of plant bugs were comparatively resistant to insecticidal treatment until the advent of DDT. Standard-strength 0.1% DDT orchard sprays were found to control *Plesiocoris nigricollis* on apple in England.[145] Sprays of 0.15% DDT gave good control of *Rhoecocoris sulciventris* on citrus in Australia, although the kill was slow and incomplete.[217] Again DDT has given satisfactory control of *Calocoris norvegicus* on strawberries in Canada. DDT in 3% dusts or 0.04% suspensions controlled the garden flea hopper (*Halticus bracteatus*) where pyrethrum failed to do so.[433] Excellent results have been obtained with aerosols containing DDT, DDD, or PCH.[429] DDT proved to be a highly effective substitute for nicotine to control the apple red bug (*Lygidea mendax*) in calyx sprays, where thiocyanates and

dinitro compounds had been ineffective.[116] In the United Kingdom, DDT is the standard treatment for the control of the apple capsid bug.[359] The tarnished plant bug (*Lygus pratensis oblineatus*) was formerly controlled somewhat inadequately by sulphur, nicotine, or pyrethrum,[291] as was *L. campestris*.[2] Sabadilla had proved superior to pyrethrum.[7] Excellent control of the former species on potatoes was attained by 1% DDT dust, although mortality took several days to develop.[190] Quick kills may be obtained with DDT aerosols.[433] Infestations of *L. hesperus* and *elisus* on seed alfalfa may be over 90% controlled by the application of 3% DDT dust at 20 lb/acre just before blossom time.[258] Species of *Adelphocoris*, such as *rapidus*, *lineolatus*, and *superbus*, may also be controlled by DDT, but as with *Lygus* the slow kill may make the results appear erratic.[19] Parathion and chlordane are no less toxic than DDT to *L. oblineatus* on alfalfa.[437] Populations of *L. oblineatus* responsible for cat-facing on peaches may be controlled to a large extent by 0.1% DDT sprays;[394] sabadilla, BHC, or chlordane is relatively ineffective.[90] In Indiana, however, chlordane sprays have completely controlled *Lygus* but not the pentatomids also responsible for cat-facing.[277a] Infestations of *Lygus* and *Adelphocoris* on cotton were controlled better by DDT than by the usual calcium arsenate treatment;[16] a 4% DDT dust almost completely controlled *L. hesperus* on California cotton,[387] the kills being speeded by the addition of sulphur.[19] Nevertheless BHC is considered to be superior to DDT for mirids on this crop,[16] although a 3% lindane content is required to ensure effectiveness in a dust.[21]

The cotton flea hopper, *Psallus seriatus*, was originally treated with dusts of calcium arsenate and sulphur. DDT dusts lightly applied achieved no better than the 80% control given by the arsenical.[148] But if applied frequently, or in high concentration (10%), DDT dusts will give better control (95%) and higher cotton yields[19] than sabadilla, thiocyanates, or calcium arsenate plus sulphur.[60] Effective control may be obtained with dusts of 2% chlordane, 10% toxaphene, 10% BHC, or 5% DDT with sulphur. Although 5% toxaphene is inferior to 5% DDT, 10% toxaphene is equally effective and gives a higher yield due to superior control of other insects.[321] Dusts of 3% DDT can eliminate severe infestations of *P. ancorifer* on onions.[18] The mirids

Sahlbergiella and *Distantiella* infesting cacao pods in West Africa were controlled by strong DDT emulsions, the application of which was limited, because of its phytotoxicity to pods, to strategic points on the stems.[418]

TABLE 2. ORGANIC INSECTICIDES FOR INSECTS AFFECTING SEED ALFALFA [437]

Average population per 20 sweeps 4 weeks after treatment

Treatment	*Empoasca*	*Agallia*	Cercopids	*Lygus*	% Yield
DDT, 2 lb/acre	6	0.5	9	4	185
Chlordane, 1 lb/acre	352	10	6	5	75
DDT-chlordane, 1.5 lb/acre	10	2	5	2	202
Parathion, 0.5 lb/acre	12	0.25	6	6	179
Untreated	113	4	13	25	100

Crops grown for seed may now be protected by DDT dusts from the attentions of *Lygus* spp., whose feeding stunts the inflorescences. Pyrethrum and sulphur dusts were previously employed. Sabadilla is also effective in this regard, but DDT is superior by virtue of its residual action (see Table 2). An application of 30 lb/acre of 4% DDT dust to a seed crop of alfalfa as it comes into full bloom was found in California to give excellent control of the population of *Lygus* before it can cause damage.[391] In Illinois, both DDT and sabadilla dusts reduced populations of *L. oblineatus* and *Adelphocoris* spp. on seed alfalfa, but the seed yield was increased only with DDT and not with the sabadilla treatments.[289] Treatment of guayule with 30 lb/acre of 2.5% DDT dust was found to kill most of the *Lygus* and raise the proportion of filled seed from 14% up to 41%.[363]

Lace bugs infesting shade-tree foliage, *Gargaphia tiliae* and *Corythucha ulmi* and other spp., have been controlled by sprays of 0.1% nicotine sulphate in soap solution.[222] The oak lace bug *Corythucha arcuata* may be controlled by DDT or lindane suspensions, which are superior to nicotine sulphate.[256a] *C. cydoniae* has been found to be more susceptible to DDT than to chlordane or BHC [121] and may be killed by DDT dusts.[19] The eggplant lace bug *G. solani* may be readily eliminated by aerosols of DDT.[319]

The larger Homoptera

When occasionally adults of the periodical cicada (*C. septendecim*) attack orchard trees, they may be 90% controlled by a 0.15% spray of HETP or TEPP; curiously enough, parathion and the chlorinated hydrocarbons proved to be ineffective.[108,439] The membracid *Glossonotus crataegi*, the quince tree hopper, is completely eliminated by standard DDT orchard sprays.[433] The buffalo tree hopper (*Ceresa bubalus*), which may infest orchards in grass, was formerly attacked unsuccessfully by oil sprays. DDT in 0.2% suspensions controlled no more than 57% of the nymphs, but 0.3% suspensions gave complete control of the adults.[158]

The cercopid *Philaenus leucophthalmus* has been combatted by DDT, aerosols giving complete control on peas,[433] and dusts or sprays being adequate on strawberries.[368] On the latter crop, however, DDT has given inferior results to those obtained with rotenone or nicotine, whereas a 0.15% spray of BHC (6% gamma) gave nearly perfect control.[327] On alfalfa this species, known as the meadow leaf hopper, was completely controlled by 0.1% chlordane sprays, which were more effective than either DDT or BHC; HETP was ineffective.[57] Recently toxaphene has proved superior to DDT, chlordane, or BHC at the 1.5 lb acre level.[56] The pine spittle bug (*Aphrophora parallela*) was formerly combatted with sprays containing pyrethrum. Recently spittle bugs of this genus infesting conifers have been controlled with DDT emulsions.[222] It has been found that, for the control of spittle bugs on alfalfa, chlordane and parathion are superior to DDT.[137] The sugar-cane frog hoppers *Tomaspis saccharina* in Trinidad and *T. flavilatera* in British Guinea are readily controlled by dusts containing DDT or BHC.[45,331]

The cicadellid or jassid leaf hoppers, which were formerly treated with nicotine, rotenone, pyrethrum, DNCHP, thiocyanates, or Bordeaux mixture, are now readily and completely controlled by DDT. The potato leaf hopper (*Empoasca fabae*) is an important insect pest on which DDT has given outstanding results.[113] Excellent control is given by 0.1% sprays (emulsions being more effective)[160] or by 1–3% dusts.[71,72] Since this species is especially prone to migration, the duration of the effect

of DDT is rather limited, necessitating several applications[190] (Table 3). A single application of 3% DDT dust at 45 lb/acre

TABLE 3. EFFECT OF DDT ON POTATO INSECTS[190]

Per cent reduction at given periods after dusting at 25 lb/acre

		Epitrix	*Empoasca*	*Lygus*
1% DDT	2 days	95.4	80.0	68.6
	6 days	83.1	10.9	85.8
2.5% DDT	2 days	98.7	80.6	66.6
	6 days	89.1	22.6	85.8

has controlled infestations of *E. fabae* in apple nurseries. Sabadilla is highly effective against *Empoasca;*[7] although more expensive than DDT, it involves less hazard to the consumer for edible crops such as beans. Parathion is extremely toxic to the potato leaf hopper, complete kills being obtained with 0.0012% sprays,[368] although its field performance is no better than DDT.[437] Toxaphene is as good as DDT in sprays for this insect,[325] but BHC and chlordane are ineffective.[410] These insecticides show similar effects on the clover leaf hopper *Agallia* infesting seed alfalfa[137] (see Table 2). Neither aldrin nor dieldrin are effective against *Empoasca*.[29a] The other leaf hoppers infesting potato, *Macrosteles divisus* and *Aceratagallia uhleri*, are also controlled by DDT.[223] Aerosols containing DDT have eradicated *M. divisus* from lettuce, and *A. sanguinolenta* from both lettuce and potato.[153] The use of DDT dusts renders it possible to grow lettuce 90% free of the aster yellows (*Chlorogenus*) disease which *M. divisus* transmits.[32,53]

For control of grape leaf hoppers (*Erythroneura comes* and other spp.) DDT is superior to nicotine, pyrethrum, thiocyanates, or BHC. Complete control has been obtained with a single spray containing only 0.01% DDT.[88,102,368] Control of nymphs and adults may also be obtained with DDT dusts.[398] Fine sprays and aerosols (applied at 5 gal/acre of 0.6% DDT solution) have proved superior to dusts, and the deposits on the foliage remain highly toxic to *Erythroneura* while not reducing the population of predators and parasites.[163,249] DDT aerosols emitted by the TIFA generator have been used successfully to control *Erythroneura* and *Dikraneura* in vineyards.[119] The less hazardous DDD

is as effective an insecticide as DDT but is less persistent; however, if the single application of DDT is made just before flowering, the residue problem on the fruit may be avoided.[163] The apple leaf hopper *Typhlocyba* is controlled by the 0.1% DDT sprays now applied in orchards.[296] The change from the lead arsenate to the DDT schedule has resulted in much better control of the leaf-hopper population.[88] DDT dusts control the corn leaf hopper (*Peregrinus maidis*) as completely as pyrethrum flowers ever did.[433] The beet leaf hopper (*Circulifer tenellus*), vector of curly-top disease, may be controlled, sufficiently to get an average stand of 95% of the beets, by 12 dustings of 10% DDT at 15 rising to 30 lb/acre.[131]

Psyllids, aleyrodids, and phylloxerids

The pear psylla (*Psyllia pyricola*) has been combatted by winter applications of a dormant oil or tar distillate.[291] The addition of 0.1% of the sodium salt of DNOC to 2% dormant oil emulsions gave excellent control of winter eggs and adults.[206] Recently a 0.1% aqueous solution of *DN-289*, applied as the buds show green tips, has proved highly effective.[208] The pear psylla is one of the orchard insects which show a relative lack of susceptibility to DDT.[368] For summer application, sprays and dusts containing nicotine or rotenone have been employed in the past. Neither BHC nor DDT is as effective as rotenone.[16] HETP is as good as rotenone initially, but is inadequate for lasting effect.[79] Toxaphene is as decisive and persistent as rotenone, but chlordane is comparatively ineffective.[205] Parathion is more toxic than HETP, is easier to handle, and has a considerable residual activity.[307] Complete mortality is achieved by 0.02% sprays, and two applications of this parathion suspension give excellent control for the season. Under greenhouse conditions, a 0.001% spray of parathion was found to give virtually complete kill of the nymphs, and a 0.045% spray killed 100% of the eggs.[368] When judged by the degree of control 1 month after application, parathion, toxaphene, and rotenone emerge as the best insecticides for the pear psylla, all being superior to nicotine sulphate; the hexahydrate of the fungicide *Dithane* is also highly effective.[79] The potato psyllid *Paratrioza cockerelli* is controlled

adequately enough by the standard DDT treatments applied to control the other potato insects.[223]

The grape phylloxera (*Phylloxera vitifoliae*) is a problem only where European rootstocks are used, which is now rare. In such cases control may be obtained by soil fumigation with carbon disulphide[291] or dormant sprays with tar distillate.[170] In South Africa the vines are fumigated during winter days with gasproof tents.[381] The greenhouse whitefly (*Trialeurodes vaporariorum*) is normally controlled by cyanide fumigation. When sprays were undertaken, nicotine sulphate, rotenone, or a thiocyanate was used.[291] The whitefly is now readily controlled by aerosols of HETP, parathion, or DDT. Complete control is obtained with 0.015% parathion sprays, and almost complete control with 0.15% DDT emulsions. BHC is as effective as DDT, but chlordane is inferior.[410] DDT is also effectively employed to control the aleyrodid *Aleurothrixus* on citrus in Argentina, and has proved the most effective insecticide for the iris whitefly (*Aleyrodes spiraeoides*) in Washington state.[173a]

Aphids

The usual method of controlling aphids has been to spray with 0.1% nicotine sulphate in 0.5% soap solution; rotenone preparations are also effective but more expensive. DDT is no more effective than nicotine, but BHC is superior; HETP is a more decisive aphicide, and parathion has residual properties in addition. The comparative effectiveness of these materials is shown in Table 4; only in the case of the potato aphid does DDT give first-rate control, although it is adequate for treatment of the pea aphid.

TABLE 4. Comparative Effectiveness of Insecticides for Aphid Control

Cotton aphid	*Aphis gossypii*	Parathion > Nicotine, BHC, toxaphene > DDT
Cabbage aphid	*Brevicoryne brassicae*	Parathion > HETP > Nicotine > DDT
Turnip aphid	*Rhopalosiphum pseudobrassicae*	Parathion > BHC > Nicotine > DDT
Pea aphid	*Macrosiphum onobrychis*	Parathion, HETP, BHC > nicotine, DDT, rotenone
Potato aphid	*M. solanifolii*	DDT, BHC > nicotine, rotenone
Tobacco aphids	*Myzus persicae et al.*	Parathion > HETP > BHC > nicotine > DDT
Woolly apple aphid	*Eriosoma lanigerum*	Parathion > BHC > nicotine > HETP > DDT

When the aphids are found on perennials such as orchard trees, an effort is made to reduce their population in the winter by destroying the eggs, employing dormant sprays containing tar-distillate phenols or dinitrocresols. These dormant sprays may be in the form of a miscible oils, soluble carbolineums, oil emulsions containing DNOC or DNCHP, or aqueous solutions of DNBP. Some phenolic substance is required to penetrate and kill the embryos within the eggs, neutral oils being ineffective in this regard.[260] The reaction of the spray must be acid for full effectiveness of these dinitrophenolic compounds.[180] The susceptibility of *Aphis pomi* eggs to DNOC is such that the minimum effective dosage is 0.012% in aqueous solution; the m.e.d. for other species varies from 0.003 to 0.050%, those that hatch soonest after the application being the most susceptible.[93] Dormant sprays of 1 qt/1 gal of *DN-289*, constituting 0.07% of the active compound (DNBP) in the aqueous spray, gave 97–100% control of the eggs of *Anuraphis*, *Myzus*, and *Hyalopterus* on apple, cherry, and plum trees.[208] The addition of DDT to dormant miscible oils did not increase the control of the subsequent population of the rosy apple aphid (*Anuraphis roseus*); but it was useful in protecting planting stock of peaches from reinfestation from their roots[19]—something that DNOC, nicotine, or HCN fumigation was unable to do.[423] The summer spray schedule of DDT has been found to control *A. roseus* completely in England. Against the leaf-curling aphis (*A. padi*) on plum DDT was as good as rotenone, but both were erratic.[433] Against the black peach aphid (*A. persicae-niger*) 0.1% DDT sprays were effective enough to eliminate the aphids from the peach orchard.[122] However, DDT sprays were inferior to BHC or HETP sprays and parathion dusts, and no better than nicotine sprays; a chlordane dust was ineffective.[251] Nevertheless, provided the coverage was sufficiently thorough, DDT proved capable of eliminating the walnut aphid (*Chromaphis juglandicola*)[294] but this species is best controlled by nicotine, TEPP, or parathion.[292b]

The black bean aphid (*Aphis rumicis*) is controlled in the garden by nicotine sulphate, and nicotine dusts are superior to DDT dusts. DDT aerosols were able to kill exposed individuals of the corn-leaf aphid (*A. maidis*) but not those within rolled leaves.[44] Sprays containing 0.1% DDT had little effect on the grape-vine

aphid (*A. illinoiensis*)[146] The melon aphid (*A. gossypii*) is controlled by nicotine but not by DDT, since the latter destroys its predators.[19] Parathion is even more destructive to the predators.[292a] In the case of *A. gossypii* when appearing as the cotton aphid, it proved impossible to obtain more than 40% mortality with DDT dusts.[133, 19] The addition of 0.1% nicotine to the calcium arsenate dusts used for cotton was sufficient to keep the aphid from becoming a problem; 0.75% rotenone could be substituted.[48] Once infestations have developed, 3% nicotine in the calcium arsenate gives effective control; sulphur dusts are also useful.[242] Under normal conditions a nicotine content of 0.5–2% in calcium arsenate is satisfactory.[147] More recently, toxaphene, BHC, or parathion may be substituted to give excellent control of severe infestations.[21] Dusts containing 1% parathion are superior to 2% nicotine or 3% gamma-BHC dusts.[27] Soil treatments with the systemic insecticide OMPA at 4–8 lb/acre, or foliage treatments at 1 lb/acre, eliminated infestations of *A. gossypii* on cotton.[243a]

The cabbage aphid (*Brevicoryne brassicae*) has been satisfactorily controlled by nicotine dusts or sprays. To preserve the parasites, the best field practice is to emit the nicotine alkaloid under a drag sheet, where it volatilizes and acts as fumigant; 87–99.9% control may be attained by treatment at 3 lb/acre with an exposure period of 1 min.[357] DDT is less effective than nicotine against the cabbage aphid, although 1% dusts[122] or 0.05% sprays have given adequate control. The organic phosphates HETP and TEPP have been found to give good control where DDT and nicotine were unsatisfactory, and parathion proved excellent.[175] HETP dusts (5%) and sprays (0.1%) have decisively eliminated populations of the cabbage aphid, whereas nicotine sprays and dusts gave only 80% control.[62] The mealy plum aphid (*Hyalopterus arundinis*) has been treated with dormant oils and nicotine according to standard methods; DDT was definitely inferior to nicotine against this species on beans.[143] However, it was controlled on peaches in Italy by 0.1% suspensions of DDT, the effect being equal to and more lasting than that of nicotine.[177] On plums in Spain, 0.02% lindane gave 99% control as against 98% with 0.05% nicotine.[76]

The turnip aphid (*Rhopalosiphum pseudobrassicae*) has been controlled successfully with nicotine. DDT treatments proved notably inferior to nicotine and to rotenone.[19, 133] Dusts of 1% parathion or lindane have proved to be excellent, the former being superior at the lower concentrations; on the other hand, with 3% nicotine or 0.1% pyrethrins the control is only transitory.[132] The apple-grain aphid (*R. prunifoliae*), a minor pest in orchards, is controlled by nicotine, DDT, or BHC.[76, 133] The green chrysanthemum aphid (*R. rufomaculatum*) is readily controlled by DDT aerosols in greenhouses.[433] It is also extremely susceptible to parathion, being virtually eradicated in greenhouses by 0.001% sprays.[368] The chrysanthemum aphid *Macrosiphoniella sanborni*, along with *Myzus persicae*, may be controlled in greenhouses by DDT aerosols, but *Macrosiphum rosae* and *Aphis gossypii* are not. HETP, TEPP, and parathion aerosols, applied at 1 mg/ft^3 of active compound with methyl chloride propellent, are able to kill all species of greenhouse aphids.[383, 384, 385]

The control of the pea aphid (*Macrosiphum onobrychis* = *Illinoia pisi*) has been carried out by dusts containing nicotine, rotenone, or one of the *Lethane* thiocyanates; rotenone is the most effective of the group. DDT has proved to be an important insecticide for the pea aphid, but it has given inconsistent results. A careful series of tests with DDT in pyrophyllite demonstrated that 100% mortality could be expected at strengths over 0.6% in the dust,[133] the DDT being at least as toxic as rotenone. Yet, in one investigation, 3% DDT dusts gave poor control whereas rotenone and nicotine gave excellent control, and DDT emulsions made for a rapid increase in population a week after the application.[19] In California, 4% DDT dusts in sulphur were found to be more effective than thiocyanates or nicotine.[267] Yet when applied from aircraft 1% DDT dust achieved only 21% control, as against 86% when 2% thiocyanate was added to the dust.[11] The toxicity of DDT dust may be enhanced by the addition of oil; when 2% oil was added to a 3% DDT dust it gave 90% control, the equal of a 0.75% rotenone dust with oil, and the protection was more lasting than with rotenone. DDT applied in aerosols propelled by methyl chloride, at the dosage of 0.5 lb/acre, has given excellent control of the pea aphid in Mary-

land,[126] as also have concentrated sprays of 20% DDT in oil solution applied by a blower.[341] DDT dusts with added oil, and DDT emulsions, are slightly more effective than the aerosols. Under these conditions DDT is a better insecticide for the pea aphid than rotenone and is not surpassed by BHC, HETP, or parathion.[13, 136] Although in laboratory tests chlordane has proved more toxic than DDT, in field applications it is decidedly inferior.[410]

The potato aphid (*M. solanifolii*) originally required special treatment with sprays of rotenone or nicotine in soap solution. Now it may be controlled by the 0.1% DDT sprays or 3% dusts employed against other potato insects,[63, 71] the results being equally as good as those formerly obtained with rotenone.[200] Emulsions are more effective than suspensions, which are superior to dusts.[1] DDT aerosols applied at the rate of approximately 10 lb/acre achieved good control of this and other aphid species infesting potatoes.[433] BHC formulations also have proved effective against potato aphids.[43, 315] The rose aphid (*M. rosae*) has been controlled by spraying or fumigating greenhouses with nicotine.

The green peach aphid (*Myzus persicae*) may be completely eliminated from peach trees by the usual 0.1% DDT sprays.[312] On potato it is controlled by the standard DDT dust schedule as thoroughly as it used to be by rotenone. Cabbage requires nine applications of 1% DDT dust for complete control.[422] DDT aerosols are significantly more effective than DDT dusts.[433] The organic phosphates HETP, TEPP, and parathion were found to be much better than DDT when combatting this aphid on celery.[173] BHC was effective in controlling *Myzus* on spinach, since its fumigant action enabled the insecticide to penetrate all crevices of the foliage.[243] For treatment of *M. persicae* and other aphids on tobacco, parathion is the favoured insecticide. Nicotine, a comparatively expensive material, is not effective at the dosages which the grower can reasonably afford. HETP and BHC are effective, although the latter has proved unsatisfactory on occasion. But a 1% parathion dust is superior to 10% DDT or 1.5% lindane, and five dustings with it give complete control.[25, 166] Parathion has not only the fumigant action which "forgives" poor coverage but also has residual qualities.[129] It is

also effective when applied in sprays at 0.2 lb/acre by mist blower or aircraft.[414] TEPP is also a favoured insecticide for quick clean-up of late-season infestations.

For the aphid *Pentalonia* on banana, the new insecticides HETP, BHC, and DDT proved to be no more effective than nicotine.[393] The yellow sugar-cane aphid *Sipha flava* was more resistant to DDT than its susceptible predators, resulting in a sixfold increase in population after a treatment.[453] Infestations of the green bug (*Toxoptera graminum*) are strikingly eradicated by parathion at 0.25 lb/acre.

The woolly apple aphid (*Eriosoma lanigerum*) is primarily controlled by the hymenopterous parasite *Aphelinus*. However, soil fumigants such as PDB and naphthalene have been applied to kill overwintering nymphs.[291] Summer sprays to control nymphs and adults contain nicotine and are applied at high pressure, impact and fumigant effect being necessary to overcome the protection of the insects' waxy covering. Not even HETP bids fair to replace nicotine in this respect.[284] Xanthone is effective, probably because it prevents the aphids from settling. Applications of DDT give inferior control of *Eriosoma* and reduce its parasitism by *Aphelinus;* the resulting increase in numbers of the aphid requires the further application of nicotine bentonite or xanthone to correct the DDT schedule.[310] BHC is an effective aphicide, but its use is of necessity confined to the early season in order to avoid tainting the crop; however, it has a place in the control of infestations in nurseries.[172a] Its toxicity is greatly increased when used in 0.5% oil emulsion.[368] Parathion is highly effective, requiring only a single application with 1 lb of the 15% wettable powder per 100 gal of spray. HETP is also effective, and its rapid breakdown eliminates all residue hazards; but being a liquid it is less easy to handle than a powder.[307]

The control of aphids on vegetable crops has recently been undertaken by systemic insecticides which are absorbed into the sap, thus avoiding the destruction of aphid predators and parasites. The material marketed in England is *Pestox III*, which contains bis(bisdimethylaminophosphonous) anhydride.[359] In addition to aphids, this systemic insecticide can also control coccids, aleyrodids, and typhlocybids by such means. The application of 3 lb/acre of this material in 0.2% aqueous solution to

a field of brussels sprouts gave about 70% control of *Brevicoryne brassicae*, and there was evidence that this degree of protection could be maintained for 7 weeks. Treatment of hops at 1.5 lb/acre gave complete control of *Phorodon humuli* for more than 6 weeks.[358] But such systemic treatments gave no protection against chewing insects such as *Pieris* and *Phyllodecta*.[287] More strongly systemic compounds such as bis(dimethylamino)fluorophosphine oxide and bis(β-fluoroethoxy) methane can control beetles and caterpillars as well as aphids, but they are too toxic for the treated crop to be consumed by human beings.[280, 281]

Attempts to control aphids and scales by systemic treatments actually date back to World War I. Control of *Aphis rumicis* on broad beans had been achieved by treatment of the soil with pyridine, $MgSO_4$, $BaCl_2$, or KCN, although the last two compounds proved toxic to the plants also.[110a] Infestations of *Eriosoma lanigerum* were removed from apple trees by injection of $BaCl_2$ or K_3AsO_3 into the trunk,[119] and injections of Spanish broom with KCN eliminated the scale *Icerya purchasi*.[370a] However, attempts to control *Gossyparia spuria* by injection of elm trees with strychnine sulphate met with no success.[370b]

Coccids

Scale insects and mealy bugs are difficult to control because of their relative resistance to contact insecticides and fumigants. In nature a high parasitism keeps their numbers down, but this may be eliminated by spray programmes outdoors or by introducing the scales into greenhouses. Scale infestations were formerly controlled in the field by lime-sulphur sprays or by 2% emulsions of dormant oil or summer oil; tent fumigation with HCN has also been practised. Greenhouses were treated by spraying with nicotine or fumigating with HCN or nicotine. As examples of field treatment, winter Volck and tar distillate are used as dormant sprays against the cottony-cushion scale (*Icerya purchasi*) in Egypt, dormant oils of high viscosity index against the San José scale (*Aspidiotus perniciosus*), light petroleum oils against the apple mealy bug (*Phenacoccus aceris*) in British Columbia,[279] and HCN fumigation against the greenhouse Orthezia (*O. insignis*) on citrus in Rhodesia.

With the advent of DDT, this insecticide was applied to mealy bugs with the oil emulsions, in the hope that it would increase the degree of control. Emulsions of 0.3% DDT containing 0.6% benzene achieved complete control of *Phenacoccus gossypii*.[364] Suspensions of 0.05% DDT killed 98% of the European elm scale (*Gossyparia spuria*) on elm trees.[117] Otherwise the standard 0.1% DDT suspension sprays were toxic only to the young crawlers of the apple mealy bug (*Pseudococcus comstocki*), the mature females being resistant.[204] The appearance of parathion offered great promise of mealy-bug control, 0.025% suspensions achieving excellent control of the apple mealy bug. The grape mealy bug (*P. maritimus*) is little affected by 0.1% DDT sprays;[156] but infestations of it on yew were completely controlled by 0.03% parathion suspensions, and 99% killed by thiocyanate sprays, while HETP, BHC, chlordane, or toxaphene gave only one-half or one-third control.[305] DDT aerosols killed less than 25% of the citrus mealy bug (*P. citri*), the adults remaining unaffected;[433] whereas the pineapple mealy bug (*P. brevipes*) was completely controlled for 4 weeks by the application of parathion in a dilute 1% dust.[318] In the greenhouse, DDT aerosols affected only the young mealy-bug crawlers; HETP completely controlled *P. citri* and *Phenacoccus gossypii* but not *P. maritimus;* while parathion killed all species.[386] Sprays of 0.015% parathion completely eliminated infestations of *P. maritimus, citri, adonidum,* and *gahani*.[312] The cottony-cushion scale *Icerya* on peaches may be controlled by two sprays of 0.03% parathion, but for safety to the consumer they must not be applied later than 30 days before harvest.[23]

The soft scales are less resistant to insecticides than the armoured ones. The black scale (*Saissetia oleae*) is adequately controlled by the addition of rotenone to the oil emulsions employed, and DDT can raise the control to 100%. Even suspensions of DDT are toxic, the young crawlers being unable to settle on treated surfaces; BHC is ineffective in this regard.[399] Infestations of this scale in greenhouses were controlled by 0.1% DDT emulsions where nicotine sulphate had failed.[21] A species of *Lecanium* (probably *quercifex*) infesting blueberries, which could be almost eliminated by DNOC or dormant oil, was similarly controlled by summer emulsions of DDT, but because of the

destruction of parasites and predators the infestation returned in late summer.[377] *Asterolecanium minus* infesting oak in California was decisively reduced by 1.5% toxaphene in 2% summer oil emulsion.[342a]

Scale insects infesting citrus orchards are usually controlled by fumigating with hydrogen cyanide at the rate of 20 cc liquid HCN per 100 ft^3 enclosed by the tent over the tree. Because of the bulky equipment required and the appearance of cyanide-resistant races of *Saissetia*, *Coccus*, and *Aonidiella*, this practice is being replaced in California by spraying with emulsions of a light-medium oil (52–70 SSU and 80–95% U.R.), which, however, does not always give satisfactory control. In Australia, where no resistance has appeared, cyanide fumigation is preferred since it is fast and thorough, and because the trees will not tolerate more than 2.5% of white oil in emulsions. In New Zealand, citrus scales have been controlled by summer oil designed for mite control in apple orchards.

The addition of DDT to the oil is more profitable than adding rotenone for control of the California red scale (*Aonidiella aurantii*), but after a few months the population reduction is not much greater than with the oil alone, because DDT, although it prevents the settling of crawlers, is relatively ineffective against the adults of this armoured scale.[142] DDT dusts are of little value, but oil solutions of DDT, if the trees will tolerate them, are quite effective. Recently a 3% kerosene emulsion, safened by aluminum stearate, containing 0.3% DDT and applied twice, has given the best control.[143] DDT is satisfactory for control of citricola scale *Coccus pseudomagnoliarum*, but is not recommended for yellow scale (*Aonidiella citrina*), for which lime-sulphur or petroleum oil is preferred. With the purple scale (*Lepidosaphes beckii*) the addition of DDT to the oil emulsions increases the control and may raise it to 90% of the young crawlers, to reduce the infestation in the following year to 5% of the one previous.[272] If rotenone is added to the DDT and oil, an almost complete kill of the immature stages may be attained.[137] With the fig scale (*L. ficus*) DDT emulsions induce leaf fall, and the most suitable application is a 2% emulsion of light summer oil.[36] With the oystershell scale (*L. ulmi*), for which dormant oils are ineffective, complete control may be

achieved if the young crawlers are hit in mid-June (Wisconsin) with a single spray of 0.1% DDT suspension.[316]

The addition of DNOC or DNCHP to the dormant oil is fairly effective against this species and the scurfy scale (*Chionaspis furfura*).[291] The substitution of 1% *DN-289* in an aqueous base gives 96 to 100% control of eggs of *Lepidosaphes*, *Chionaspis*, and the San José scale (*Aspidiotus perniciosus*).[208] This last species has been controlled by lime-sulphur sprays in eastern North America, as has the red scale in Australia. Harvested fruits infested with the San José scale are fumigated with hydrogen cyanide or methyl bromide before shipment. Methyl bromide is favoured for fumigating nursery stock infested with this scale, although HCN allows shorter fumigation periods and consequently less hazard of phytotoxicity.[37]

It has recently been established that parathion effectively controls the purple scale, citricola scale, yellow scale, California red scale, cottony-cushion scale and the black scale.[31a] However, the soft brown scale (*Coccus hesperidum*) and the late immature "rubber" stages of the hemispherical scale (*Saissetia hemisphaerica*) survive 0.025% suspensions of parathion.[342] Armoured scales may be controlled in greenhouses by parathion, 0.015% sprays of which can completely control *Diaspis*, *Pinnaspis*, *Parlatoria*, and *Chrysomphalus*, although the adult mortality is slow.[342] Parathion sprays are much more effective than HCN fumigation or oil sprays to control the olive scale (*Parlatoria oleae*), being especially toxic to the eggs and young stages.[397]

Thysanoptera

Control of thrips has been commonly obtained by spraying an inorganic stomach insecticide baited with brown sugar. The greenhouse thrips (*Heliothrips haemorrhoidalis*) has been controlled with sweetened bait sprays containing Paris green, by rotenone sprays[448] or dusts, or by fumigation with naphthalene or hydrogen cyanide.[291] DDT aerosols, sprays, or dusts have given good results against this species and *Hercinothrips femoralis*. Lindane is 10 times as toxic as DDT to *H. haemorrhoidalis*, whereas toxaphene and chlordane are less toxic.[342] Aerosols are effectively employed to control thrips infestations in greenhouses. Most species of thrips except *F. tritici* are

controlled by 5% DDT aerosols applied at 100 mg ft^3, while 10% HETP aerosols at 10 mg/ft^3 control all thrips except those in concealed places; parathion at the same dosage gives complete control.[386] Parathion in 0.015% sprays completely controls *H. haemorrhoidalis* and *H. simplex*.[312] Thrips infesting carnations or other cut flowers are susceptible to treatment with selenium applied to the plants through the soil. The application of sodium selenate at the rate of 0.5 gm/ft^2 controls the thrips infesting greenhouse chrysanthemums.[164]

The flower thrips of citrus (*Frankliniella cephalica*) has been controlled by sulphur dusts or lime-sulphur sprays. Dusts of DDT have been found effective to control *F. moultoni* on grape,[296] and other species of this genus on onion as well as on grape.[18] In tests involving *F. fusca* on peanut, DDT sprays were found to increase the yield by 35%, as against 21% for tartar emetic and 7% for pyrethrum.[339] *Frankliniella tritici* on cotton may be controlled by BHC or toxaphene dusts or DDT sprays, DDT dusts and tartar emetic sprays being ineffective.[168]

The pear thrips (*Taeniothrips inconsequens*) has been controlled in the past by oil emulsions of nicotine applied before the opening of the buds.[291] It has been found that DDT suspensions and emulsions have given almost complete control of this thrips, both on the foliage of plum[19] and on the vegetation beneath the trees.[150] Benzene hexachloride is definitely less effective.[16] A dormant spray of DDT is the best method so far discovered for controlling pear thrips in British Columbia.[265] DDT aerosols have given almost complete protection against the gladiolus thrips (*T. simplex*) in greenhouses.[383] Chlordane, toxaphene, and BHC are also highly effective; but as far as sprays are concerned it is not invariably found that the chlorinated hydrocarbons are superior to tartar emetic for this species.[110, 383, 433] Either DDT or BHC is employed to obtain satisfactory control of *Taeniothrips* on greenhouse carnations in the south of France.[216] Before the advent of DDT, *Liothrips oleae* got so far out of hand in Spain that a million olive trees had to be fumigated with HCN in 1945–46.[179]

The onion thrips (*Thrips tabaci*) was formerly somewhat resistant to control, tartar-emetic bait sprays, nicotine sprays, and naphthalene dusts having been employed.[291] Either rote-

none or DNCHP, like nicotine sulphate, gives about 90% control. Suspensions or emulsions of DDT have usually proved superior to tartar-emetic bait sprays, although cases are recorded where DDT was no better and one case where it proved to be inferior.[130, 433] Work in Colorado, Massachusetts, Utah, and California has shown DDT to be as good an insecticide as any, the most effective formulations being either emulsions or dusts admixed with sulphur.[266] DDT in aerosols gave effective control of *T. tabaci* and *T. nigropilosus*.[443] BHC dusts containing 0.5% gamma isomer gave excellent control of *T. tabaci* on both onion and tomato,[315] although slightly inferior to DDT.[226] Curiously enough, BHC was more effective against this species on cotton; whereas in dusts applied to onion one-third as much of the gamma isomer (lindane) was required as DDT, with *T. tabaci* on cotton only one-thirtieth as much lindane as DDT was required, 0.18% lindane dusts being as effective as 5% DDT dusts.[92] Chlordane is also highly toxic to onion thrips.[410] When used as 5% dusts on cotton, toxaphene proved definitely superior to DDT, chlordane, or DDT-BHC mixtures.[153] In sprays on onions, a mixture of 0.1% DDT with 0.2% nicotine was found to be more effective than any of the chlorinated hydrocarbons, which in turn were superior to tartar emetic and nicotine alone.[130] Dusts containing 5% DDT, 5% chlordane, or 1.2% lindane are now recommended for multiple applications at 35 lb/acre;[33] 2.5% DDT suspensions are also favoured at 100 gal/acre.[27] In California the most suitable schedule was found to involve 10% DDT dusts applied at 30 lb/acre once weekly for 6 weeks, starting when the onions are 10 in. high.[435] Two applications of 1% parathion dust are also recommended, provided they are applied not later than 30 days before harvest.[23] 2.5% aldrin dusts are also superior to the 10% DDT dusts.[435a]

Control of the citrus thrips (*Scirtothrips citri*), originally attempted with sulphur, was taken over by tartar-emetic bait sprays; in California a race resistant to this treatment appeared relatively quickly, and nicotine was substituted in the bait sprays. The effectiveness of DDT was comparable to that of nicotine, and better control was obtained with sprays than with dusts.[?] Aerosols containing DDT completely controlled *S. citri* but had no effect on *Anaphothrips obscurus* in citrus orchards.[418] Par-

athion has been found to control *S. citri* effectively.[319] Dusts of either DDT or BHC were found to be very effective against *S. signipennis* on banana in Queensland.[392]

The larger Lepidoptera

Most caterpillars are readily susceptible to control by stomach poisons, because of their voracious appetite; and by contact insecticides, because of the large area of unsclerotized skin they present. The cabbage worm (*Pieris rapae*) is a typical case in point. The larvae may be destroyed by lead arsenate in 25% dusts or 0.4% suspension sprays, or by calcium arsenate or Paris green in 25% dusts, applied to the cole foliage on which they feed; but this treatment should be confined to the early part of the season to avoid residue hazards to the consumer. Pyrethrum, nicotine, and rotenone dusts may be used throughout the season without residue hazard. Of these botanicals, rotenone is the most satisfactory because of the relative persistence of its toxicity both as a contact and a stomach poison; it is applied as 4% dusts, or as 0.03% suspension sprays to which a "sticker" has been added to make it adhere to the waxy cabbage foliage.[291] DDT has proved more satisfactory than all these poisons,[433] 0.5–3% dusts and 0.05% sprays achieving complete control and improving the growth of the plants.[19] Dusts containing BHC also give complete control,[326] this material appearing even more toxic to *P. rapae* in the laboratory;[50] chlordane is inferior.[410] The results of field tests with dusts of various insecticides against *P. rapae* and *Trichoplusia* together on cabbage are shown in Table 5. Here the superiority of DDT is evident,* although the difference in control with BHC, chlordane, toxaphene, DDD, rotenone, sabadilla, and pyrethrum is not statistically significant; lead arsenate and methoxychlor are definitely inferior, whereas calcium arsenate is ineffective.[124] DDT is equally effective against *P. brassicae*.[133] The alfalfa caterpillar (*Colias eurytheme*) was formerly combatted with lead arsenate, pyrethrum, or rotenone dusts, which gave less than 50% control. Now complete control may be obtained by dusting at 25 lb/acre with 1% DDT or 5%

* Recently, dieldrin has proved slightly superior to DDT, aldrin slightly inferior [Dills and Odland, *J. Econ. Ent.*, **43**:384–385 (1950)].

DDD, or at 50 lb/acre with 1% lindane. Concentrated sprays of 2.5% DDT applied at 5 gal/acre also give complete control. Dusts containing toxaphene or TEPP are also effective, but methoxychlor is inferior.[390]

TABLE 5. INSECTICIDES IN DUSTS TO CONTROL CABBAGE CATERPILLARS [124]

(*Pieris rapae* and *Trichoplusia ni*)

Insecticide	% Concentration	% Control
DDT	3	88.2
DDD	3	87.0
Rotenone	0.75	85.8 *
Sabadilla	10	84.5
Lindane	0.4	84.2
Ryania	30	83.1
Toxaphene	3	80.8
Pyrethrum	20	78.6
Lead arsenate	20	77.6
Chlordane	3	72.6
Methoxychlor	3	60.9
Significant difference at 5% level:		14.0

* 85.8% in 1946 when *Pieris* predominated, 35.5% in 1947 when *Trichoplusia* predominated.

The sphingid larvae or hornworms infesting tobacco and tomato, *Protoparce sexta* and *P. quinquemaculata*, have been controlled with dusts containing 15% Paris green, 36% cryolite, 50% calcium arsenate, or pure powdered lead arsenate.[291] *Protoparce sexta* is the more resistant of the two species to DDT, cryolite, and insecticidal azo compounds, but the more susceptible to phthalonitrile. A dosage of DDT that kills 100% of *P. quinquemaculata* was found to kill only 22% of *P. sexta*.[400] The former species on tomato or tobacco may be readily controlled with DDT dusts or aerosols.[433] The latter species, the southern tobacco hornworm *P. sexta*, requires so much DDT (10 lb/acre in dust form or 3.6 lb/acre in spray) that the expense dictates retaining 0.8% lead arsenate sprays for control, or substituting cryolite, barium fluosilicate, or basic copper arsenate.[5] However, 10% dusts of toxaphene or DDD have been found to be more effective than cryolite against both species of *Protoparce*, while dieldrin shows promise.[129b]

The gipsy moth (*Lymantria dispar*) had been controlled on shade trees by 1% lead arsenate suspensions applied by power sprayers or by dusts of calcium arsenate thrown by power dusters. In hardwood forests, the larvae had been controlled by calcium arsenate applied from aeroplanes and autogyros at 40 lb/acre. Now this destructive caterpillar can be completely controlled with 1 lb/acre of DDT dissolved in oil, and the young larvae may be destroyed by application of only 0.5 lb/acre.[132]

The advent of DDT has rendered it possible to control extensive infestations of forest insects by spraying from aircraft. Reference has already been made to the 413,000-acre campaign against the fir tussock moth (*Hemerocampa pseudotsugata*), which obtained almost 100% control with DDT sprayed at 1 lb/acre.[147] The spiny maple worm (*Anisota rubicunda*) and its congeners may be eliminated with DDT sprayed on hardwood forest at 5 lb/acre. Emulsions of 0.1–1% DDT control tent caterpillars (*Malacosoma* spp.) and the fall webworm (*Hyphantria*) on shade trees.[434] Other forest insects such as *Lymantria monacha*, *Dendrolimus pini*, and *Panolis flammea*, which immediately before World War II were combatted in Europe and Asia by DNOC, pyrethrum, or rotenone dusted from the air, can now be readily controlled by DDT in oil solution sprayed from aircraft. The more hairy caterpillars formerly required a mordant insecticide such as DNOC, but the performance of DDT in oil solution with *Hemerocampa* shows that this is no longer a problem. However, with the excessively hairy salt-marsh caterpillar *Estigmene acraea* (the "woolly bear") on cotton, dusts of DDT, DDD, BHC, or chlordane proved ineffective, only 20% toxaphene dusts succeeding in attaining more than 90% kill.[21] Recently, dichlorodiphenyl-nitrobutane (*Dilan*) has proved decidedly superior to toxaphene against this species.[370c] Toxaphene was as effective as DDT in achieving 100% control of the eastern tent caterpillar (*M. americana*) with 0.1% suspension sprays, while 0.3% BHC sprays left 2% of the larvae as survivors.[403]

Phalaenids

As a typical leaf-eating cutworm, the cabbage looper (*Trichoplusia ni*) is readily controlled by DDT.[368] It was formerly successfully treated with lead arsenate, cryolite, or rotenone.[291]

DDT was superior to either pyrethrum or rotenone, 0.5% dusts and 0.05% sprays giving complete control.[19, 133] The results of dusting with various insecticides against both *Pieris* and *Trichoplusia* are shown in Table 5. Here rotenone is seen to be much less effective against *Trichoplusia* than against *Pieris*.[124] Chlordane is also inferior to DDT, being no better than rotenone.[410] The velvet-bean caterpillar (*Anticarsia gemmatilis*), which infests the foliage of peanut plants, may be readily controlled by DDT dusts and sprays.[433] DDT, BHC, cryolite, and ryania dusts were found to be equal in effectiveness, as judged by the increase in yield of the peanut[25] or soybean crop.[261] As judged by the number of larvae remaining, DDT, BHC, toxaphene, methoxychlor, and parathion were all far superior to cryolite; only chlordane was inferior.[25]

The cotton leafworm (*Alabama argillacea*) is an exception; although the larvae are unprotected, they are not controlled by DDT.[19] With 2% DDT dust, only 36% mortality was obtained at dosages of 32 lb/acre and no mortality at 10 lb/acre.[433] Since calcium arsenate is 3 times as toxic as DDT, this inorganic insecticide is employed in the cotton fields, being dusted 3 or 4 times at 5-day intervals at 4–8 lb/acre, a treatment designed also to control the boll weevil.[291] Other chlorinated hydrocarbons, such as BHC and toxaphene, are effective in controlling this species.[21]

The armyworm (*Cirphis unipuncta*), fall armyworm (*Laphygma frugiperda*), and southern armyworm (*Prodenia eridania*) feed on the surface of the ground. They have been controlled by inorganic poisons incorporated in water-base bran baits, which may be sweetened with 5% molasses. The insecticides formerly used were 1% of arsenious oxide, sodium arsenite, or Paris green; sodium fluosilicate is superior to arsenicals in not being repellent.[291] Against *Euxoa* in South Africa, sodium fluoride is preferred to sodium arsenite, since the latter is repellent and promotes decay of the chopped cactus used as the carrier, whereas the former delays it.[354] With *Cirphis*, sodium fluosilicate or Paris green baits may achieve over 90% control; calcium arsenate causes slower kills and cryolite is ineffective.[329] Paris green bait applied at 30 lb/acre, or calcium arsenate dusted at 20 lb/acre, gives about 90% control of this species.[275] Treatment

of cabbage with cryolite, lead, or calcium arsenate controls *Prodenia litura* in Queensland.[193] In recent years the chlorinated hydrocarbons have been developed as cutworm poisons. With *Laphygma*, DDT and BHC proved to be superior to Paris green as a bait ingredient, and chlordane was best of all.[63] DDT in 0.2% sprays or 5% dusts gave adequate to complete control on forage and truck crops. As far as sprays are concerned, laboratory and field tests have shown that BHC and chlordane are no less toxic than DDT to *Cirphis*,[50] *Prodenia*,[110] and *Laphygma*.[63] But with dusts, only DDD is as effective as DDT; BHC is nearly so, but methoxychlor, chlordane, and toxaphene are inferior.[229] Even with DDT, dusts are valueless to control *Laphygma* on sweet corn once the larvae are protected.[45] Where the fall armyworm infests cotton, it may be controlled by dusts of 20% toxaphene, 10% chlordane, 3% lindane, or 10% DDT.[21] The beet armyworm (*L. exigua*) has been completely controlled in flax crops with a 5% DDT dust applied at 20 lb/acre.[365] Climbing cutworms on peaches may be controlled by DDT dusts or sprays, BHC being effective only in dusts, and sabadilla ineffective in either form.[81]

The subterranean cutworms are difficult to attack with anything but poison baits applied in the evening before the cutworms emerge for nocturnal feeding. However, strong DDT dusts applied to the crop they frequent were found to give good control of the black cutworm (*Agrotis ypsilon*) in Europe and America.[435] Dusts containing 10% DDT or 20% toxaphene are recommended for the granulate cutworm (*Feltia subterranea*) on cotton.[21] With the pale western cutworm (*A. orthogonia*) only slight contact toxicity was shown by DDT or methoxychlor, the more active compounds in ascending order of effectiveness being toxaphene, chlordane, pyrethrins, DNOC, and lindane[66] (Table 6). With the mixture of species of cutworms attacking tobacco, formerly controlled by 2% Paris green in bran baits, 10% dusts of DDT, BHC, or sabadilla were more effective, and DDT baits were best of all.[353]

Heliothis armigera, synonymous with *H. obsoleta*, infests a great variety of crops and is variously known as the tomato fruitworm, the corn earworm, and the cotton bollworm. On vegetable crops, particularly tomato, the inorganic poisons cryolite

and calcium arsenate were used[193] since rotenone was ineffective.[55] Basic copper arsenate has been found to be twice as effective as calcium arsenate. The organic insecticide DDT has proved to be even better. The tomato fruitworm may now be controlled on a wide variety of plants with 2% DDT dusts or 0.1% DDT suspension sprays.[301] On tomatoes in Queensland, the 2% dusts needed frequent application, the best results being given by 0.2% sprays.[100] Chlordane dusts are inferior to DDT dusts and to cryolite.[157] The corn earworm is hard to control when the larvae are protected within the ears. An effective but laborious solution was the injection of hexachloroethane or mineral oil into the ear.[291] The degree of control could be made complete by the addition of DDT to the mineral oil, but it taints the corn. DDT in 3% dusts has achieved almost complete kills on occasion, being superior to chlordane and toxaphene; a 5% lindane dust is superior, but it taints markedly. The best control is given by a 40% ryania dust, which is also the most effective application for the corn borer. When applications are made as 0.25% suspension sprays, DDD is superior to DDT and ryania.[26] However, no dusts or suspension sprays are really effective against the earworm.* Solutions and emulsions of 2% DDT mineral oil, applied to the silks, give the best results short of injecting oil into the ears. DDD is even more effective and offers no residue hazard; BHC and chlordane are equally insecticidal with DDT but taint the kernels; toxaphene and methoxychlor are inferior in these solutions and emulsions.[44] Aldrin, dieldrin, and pyrethrins plus piperonyl butoxide are inferior to DDT,[84a] as also are its nitropropane and nitrobutane analogues (i.e. *Dilan*).[265a] The cotton bollworm may be controlled with dusting at 10–15 lb/acre with 10% DDT or 20% toxaphene, which is more effective than cryolite, lead arsenate, or calcium arsenate.[21] The tobacco budworm (*Heliothis virescens*) was formerly combatted by the laborious process of placing in each bud a mixture of 1.3% lead arsenate in corn meal.[291] Now it can be controlled with the 10% DDT dusts applied at 9 lb/acre for control of the tobacco flea-beetle. For the flax bollworm (*H. ononis*), DDT proved to be

* With the exception of parathion dusts, which involve hazard to the consumer [Wene and Blanchard, *J. Econ. Ent.*, **43**:1–4 (1950)].

the most toxic of 10 contact insecticides tested in the laboratory, being surpassed only by pyrethrins in toxicity[66] (Table 6).

Tortricids and olethreutids

The tortricid leaf rollers are somewhat refractory to insecticidal control because many of them live and feed within shelters or crevices. The spruce budworm (*Choristoneura fumiferana*) is a case in point. It was originally attacked with 0.3% lead arsenate from power sprayers, where fair control was achieved; and by dusting forests from the air with calcium arsenate at about 30 lb/acre, and here the degree of control was largely inadequate. DDT is much better than arsenicals and is highly toxic to spruce-budworm larvae by both contact and stomach action, surpassing lindane, DNOC, and six other insecticides (Table 6),

TABLE 6. CONTACT INSECTICIDES FOR *Choristoneura fumiferana, Heliothis ononis,* AND *Agrotis orthogonia* [66]

Median lethal deposits, $\mu g/cm^2$

Compound	*Choristoneura*	*Heliothis*	*Agrotis*
DDT	0.3	7	80
Lindane	1.9	23	5.5
Chlordane	140	Neg.	18
DNOC	4.0	16	7.5
Nicotine	42	400	Neg.
Pyrethrins	0.05	4	8.2

but the dosage-toxicity curve is very flat, so that 100 times the LD_{50} dose is required for complete control with DDT.[66] In field experiments the older and more exposed larvae showed 98% mortality where DDT was applied from aircraft at 1 lb/acre.[100] The younger larvae, which are concealed in the lightly webbed new spruce shoots, showed only 72% mortality to similar applications.[79] However, better results are obtained very early in the season, when the larvae emerge from their hibernacula. A more exposed species such as *Tortrix pronubana* in greenhouses was completely controlled by DDT but not by BHC.[343] The orange tortrix (*Argyrotaenia citrana*), a pest of raspberries in the state of Washington, cannot be eliminated by DDT, whose application also leads to outbreaks of the Willamette mite. The most effective insecticide for this species is DDD, 0.2% solutions of

which give 99% control; it is superior to any of the other chlorinated hydrocarbons, cryolite, or parathion.[367] However, parathion has been found to give adequate control of both the orange tortrix and fruit-tree leaf roller in California citrus orchards.[814]

The red-banded leaf roller (*Argyrotaenia velutinana*) furnishes another example of the inability of DDT to control protected tortricid larvae. This is normally a minor pest of apple orchards in North America, and it feeds on the undersurfaces of the leaves where they overlay apples. It had been satisfactorily controlled by the 0.3% lead arsenate spray schedule. Coincidently with the trend of 0.1% DDT schedules in New York in 1946, an infestation of red-banded leaf roller developed. It has been related to the comparative inadequacy of DDT to control the second brood when the fruits are ripening, along with the liability to DDT to eliminate its parasites.[212] A return to the lead arsenate schedule has been found to give excellent control in some cases,[174] although unsatisfactory in others.[181, 185] But the new insecticide DDD, in 0.05% emulsions or 0.003% suspensions, has consistently eliminated the second-brood larvae.[185] Parathion in 0.025% suspensions has been found to give excellent control of both broods and is effective down to 0.006% suspensions, but it does not show as great a penetration and contact action as DDD.[174, 181] Indeed a cover-spray schedule of 0.03% parathion is not significantly superior to a 0.3% lead arsenate spray programme, although much better than a 0.1% DDT schedule.[257] Toxaphene (0.1%) has given fair [174] to very good [181] results, but chlordane, TEPP, or methoxychlor is valueless.[174]

Olethreutid larvae usually can be almost completely eliminated by residual deposits of DDT contacting them before they reach a concealed habitat. For example, emulsions of 0.1–0.5% DDT achieved almost complete control of the pine tip moth (*Rhyacionia frustrana*), being a great improvement on the non-residual nicotine spray previously employed.[152] With the strawberry leaf roller (*Ancylis comptana*), formerly controlled with rotenone, cryolite, or barium fluosilicate, a 3% DDT dust proved to be superior to a nicotine sulphate spray.[19] The grape-berry moth (*Polychrosis viteana*), formerly inadequately controlled by three cover sprays of 0.4% lead or calcium arsenate, may be controlled with 0.1% DDT sprays,[88] three of which are sufficient for the

season.[156] This schedule gives residues of approximately 8 ppm on the harvested grapes; in this connexion it has been found that methoxychlor and DDT, less hazardous compounds, are almost as insecticidal as DDT. For adequate control, the DDT sprays must be supplemented with miscible oils, which increase the absorption of residues in the grape skin.[110b] Toxaphene, chlordane, and BHC are ineffective against the grape-berry moth.[104] Parathion is the only insecticide known to destroy the larvae within the grapes.[110a] The grape moth of Europe (*P. botrana*) is effectively controlled by DDT; here again BHC proved useless.[170]

The oriental peach moth (*Grapholitha molesta*) in some areas of the United States is adequately controlled by *Macrocentrus* parasites;[88] the application of DDT would jeopardize their existence, although frequently a high *Macrocentrus* population has been found to survive the DDT schedule. In Victoria, DDT has been applied because of the failure of *Macrocentrus* to establish itself, and the schedule reduces the infestation by 65%. In New Jersey, a 0.1% DDT spray schedule has been found capable of attaining an 80% reduction in fruit injury.[445] Parathion shows appreciably greater residual toxicity than DDT to larvae and adults of this species.[368] A schedule of 0.025% parathion sprays has been found slightly more effective than 0.1% DDT,[135] whereas DDD and methoxychlor are slightly inferior.[98] EPN is also effective against the oriental peach moth.

DDT has given comparatively good results against the plum moth (*G. funebrana*) in England, one application of 1% emulsion being as good as two with nicotine, and 30–40% control being achieved. The eye-spotted bud moth (*Spilonota ocellana*) on apple is highly susceptible to residual poisoning by DDT in the summer schedule.[135] The overwintering larvae may be 98–100% controlled by DNBP in dormant sprays;[208] promising results have also been given by dormant applications of BHC in oil emulsion.[208] Parathion has given excellent control, either as a delayed-dormant spray against the larvae in their hibernacula, or even better as a pre-pink spray when the larvae are at large; the former DNOC-nicotine-lead arsenate schedule achieved only 40% control.[103] Both DDD and parathion have given excellent control of the bud moth on prune.[270a] The pea moth (*Laspey-*

resia nigricana) may be controlled by a strong (0.5%) DDT spray applied at 140 gal/acre; BHC is ineffective.[444] However, lead arsenate has proved superior to DDT for the control of the Catalina cherry moth (*Melissopus latiferreanus*) on walnut in California.[294]

The codling moth

The larva of the codling moth (*Carpocapsa pomonella*) is one of the principal targets of insecticidal control, and much of insect toxicology has been motivated by the refusal of the housewife to buy wormy apples. The problem is to poison the newly hatched larva during its short journey from the twig or leaf to the external surface of the fruit or the inside of the calyx cup. The usual practice is to apply dilute (generally less than 0.5%) suspensions of insecticides in sufficient water to wet the foliage to run-off, often with appropriate spreaders and stickers. Recently very much less of more concentrated sprays has been applied in mist-spray form. For the sake of economy of labour, the insecticide is generally applied simultaneously with a fungicide such as sulphur, ferric dimethyldithiocarbamate (*Fermate*), disodium ethylene bisdithiocarbamate (*Dithane*), Bordeaux mixture, or copper oxychloride (*COCS*).

The usual procedure has been to apply a 0.2% suspension (2 lb/100 gal) of lead arsenate as soon as the petals have fallen, in order to cover the calyx cup (the petal-fall or calyx spray). Thereafter it is necessary to apply 3 or 4 cover sprays of 0.4% lead arsenate at weekly intervals until the eggs have completed hatching. Spraying has to be resumed when a second generation appears, and often a third, so that as many as 12 cover sprays have been applied in certain southern districts. So great an accumulation of arsenical requires the fruit to be washed in dilute acid after picking, unless the spray programme has been discontinued well before harvest.

Lead arsenate has maintained its position against other inorganic poisons such as cryolite or calcium arsenate, the latter being more dangerous to foliage and the former giving about the same degree of control;[112] and against organic insecticides such as nicotine bentonite (no residue hazard), xanthone (which is also a miticide),[305] and phenothiazine (which gives an extra high

degree of protection)[278] on the grounds of relative cost.[51] The effectiveness of lead arsenate may be increased by the so-called spreaders and stickers, such as fish oil, soybean oil, and phosphatides in kerosene, which are added to the spray suspension at the rate of 0.5–2 qt/100 gal. A recent synthetic sticker, polyethylene polysulphide (*p.e.p.s.*), forms a resistant film on the foliage.[232] The insecticidal activity may be increased by certain safeners, added to reduce phytotoxicity, such as lime or zinc sulphate, and by the fungicidal Bordeaux mixture. The miticide DNCHP and the fungicide-miticide lime-sulphur also reduce phytotoxicity, but decrease the insecticidal action of lead arsenate.[234]

The appearance of DDT in the orchard industry in 1945 has radically changed the picture. In nearly all experiments performed in the United States and Australia to compare 0.1% DDT (1 lb/100 gal) with 0.3% lead arsenate (3 lb/100 gal), the DDT treatment gave superior control, not only reducing the percentage of infested apples, but still more reducing the superficial injuries or "stings" made by the codling-moth larvae (see Table 7).

TABLE 7. DDT VERSUS LEAD ARSENATE SPRAY SCHEDULES FOR CODLING-MOTH CONTROL

Per cent of injured fruit: superficial injury per cent in brackets

Region	0.3% Lead Arsenate	0.1% DDT
West Virginia [296]	22.0	0.5
Illinois [425]	7.7	2.5
New York [213]	16	1
New York [54]	65	13
Virginia [235]	12–30	1–6
Maryland [183]	25 (13)	24 (4)
Delaware * [352]	7 (30)	5 (10)
Tasmania [297]	16.3	5.0
Queensland [284]	20.2	20.1

* 4 lb/100 gal lead arsenate versus 0.8 lb/100 gal DDT; cover sprays only.

When 0.1% DDT emulsion was substituted for the suspension in the Queensland experiments, the fruit infestation dropped to 7.6%. In the Tasmanian work, 0.1% emulsions reduced fruit infestation to 3.0%, a significant difference from the 5.0% with suspensions. Emulsions are considered in Switzerland to be defi-

nitely more effective than suspensions.[170] In South Australia, there was no significant difference between the two forms of spray, 0.1% concentrations being optimum for small orchards and 0.05% for large.[255] In New York, oil emulsions did not increase control.[51] A curious result was obtained in Kansas, where a 0.2% DDT emulsion left an infestation of 26 (12) as against 8 (21) for 0.4% lead arsenate, but it was claimed that the DDT concentrate was defective because of too much wetting agent.[324] Reports that the DDT schedule gives better control than lead arsenate have also been made from Illinois,[88] Virginia,[233] Queensland,[74] Victoria,[404] and South Australia;[255] a report from New Mexico has the DDT schedule as slightly less effective.[18] DDT dusts are superior to lead arsenate dusts, 5% DDT giving 91% uninjured fruit as against 77% with 30% lead arsenate; they are more effective than phenothiazine dusts and even lead arsenate sprays (90% and 86% uninjured fruit, respectively).[204] DDT also gives excellent control of *Carpocapsa* on pear in Victoria, three 0.1% sprays doing the work of four on apple.[405] It also is excellent for this species in walnut orchards in California, lead arsenate being very good.[294]

It is noted that the DDT schedule leaves the foliage brighter and uninjured, and the fruit is cleaner since the residue is not noticeable.[284] The visible residue is due to the pyrophyllite or some other inert diluent of the wettable powder,[235] most powders consisting of DDT and pyrophyllite in 50:50 proportions (50% W. P.). Whereas emulsions, whether the concentrate has an oil base [404] or volatile aromatic base (benzene or xylene),[213] are not toxic to foliage, the addition of 0.5% summer oil to the suspensions causes foliage injury,[51,88] particularly on pears,[405] or on some apple varieties when applied at the fruitlet stage. Either oil emulsions or oil added to suspensions greatly increases the invisible residue in the skin of the fruit that constitutes the hazard to the consumer.[51,235] For this reason, it is recommended that no DDT sprays be applied within 1 month of harvest; or they may be discontinued as soon as the first brood of larvae have hatched, to spare the *Aphelinus* parasites to control the late-season *Eriosoma*.[424]

The employment of the DDT schedule instead of lead arsenate has led to the rise in orchard populations of *Eulia velutinana* in eastern North America, and of *Tortrix postvittana* in eastern

Australia. It may also lead to a rise in the population of *Eriosoma* late in the season. More seriously, the use of DDT favours a build-up of leaf mites towards the end of the season, and the amount of increase has shown a correlation with the concentration of DDT employed.[352] This has been observed on apples, pears, walnuts, and citrus, and in eastern North America (*Paratetranychus pilosus* and *Tetranychus schoenei*), in the Central States (*Tetranychus* spp.),[324] the Pacific Northwest (*T. pacificus*), California (*P. citri*), south Australia (*Bryobia praetiosa*), eastern Australia (*Bryobia* and *Tetranychus*), Switzerland and England (*Paratetranychus*).[170,253] It was observed that suspensions, involving deposits of inert diluent, favoured the rise of mites more than emulsions did. So far, DDT is the only orchard insecticide that has led to the appearance of mite problems; phenothiazine has this property in a slight degree.[278] Lead arsenate, nicotine bentonite, or cryolite do not induce mite infestations, and xanthone reduces them.[308] The leaf-roller and mite problem may be simultaneously solved by the use of parathion, which is extremely effective in controlling the codling moth. However, parathion as a panacea for orchards is limited by the toxic hazards it presents to the operator. The less poisonous organic phosphate, EPN, has recently proved excellent for control of both the leaf roller and the codling moth.

For control of codling moth, BHC was found to be inferior to DDT in the United States; it failed to control mites, and tainted the fruit.[16,48,425] In Tasmania 0.1% BHC suspensions allowed 27% of fruit infestation as against 5% with DDT.[297] Chlordane and toxaphene are ineffective to control the codling moth.[12] The replacement of the DDT schedule by DDD or methoxychlor has resulted in unsatisfactory control of this insect.[313] The control of *Carpocapsa* populations in the orchard is assisted by the inclusion of DNOC with the dormant oil emulsions, reducing the infestation by 25–50%. It has recently been found in Europe that the addition of DDT to these DNOC-oil applications gives really good control of overwintering tortricid larvae.[180]

Pyralids

Most pyralid larvae are readily susceptible to control by DDT. The beet webworm of Australia, *Hymenia recurvalis*, formerly attacked with lead arsenate, is now controlled with 1% dusts or

0.1% sprays of DDT.[388] However, on a crop such as spinach, which offers a multitude of crevices, DDT gives only fair results; here BHC is the most effective insecticide, followed by pyrethrins with PCH synergist.[63] For the control of the grape leaf folder (*Desmia funeralis*) in 5% dusts, DDT proved to be the least effective of the five chlorinated hydrocarbons tested, and BHC the most. However, none of them were as good as 50% cryolite dusts, and all were surpassed by 1% parathion dust although its residual effect was transitory.[162] The cross-striped cabbage worm (*Evergestis rimosalis*) was originally controlled by lead arsenate applied early in the season, or by pyrethrum or rotenone which could be applied later. A 3% DDT dust was found to be equal to pyrethrum flowers (1.2% pyrethrins) in giving complete control, and superior to a 0.75% rotenone dust. A 0.02% DDT spray was as effective as a 0.04% rotenone spray in giving complete control within 4 days of application.[433] However, ryania and rotenone are the preferred substitutes for cryolite against the cranberry fruitworm (*Mineola vaccinii*).[374a]

The garden webworm (*Loxostege similalis*) infesting alfalfa or cotton was originally controlled by calcium arsenate. DDT has proved effective when applied in aerosols to vegetables,[433] and as sprays to cotton. On the latter crop, a 10% DDT dust is inferior to a 20% toxaphene dust or a dust mixture of BHC and DDT dust.[21] The beet webworm (*L. sticticalis*) on alfalfa in Spain is about 80% controlled by 0.1% DDT sprays; 0.15% BHC sprays are slightly more effective.[290] In the United States, a single application of 2% parathion dust at 20 lb/acre has given excellent control of beet webworm.[23]

Infestations of the European corn borer (*Pyrausta nubilalis*) are hard to control, and the larvae are susceptible to treatment only immediately after hatching. The overwintering larvae have not yet been successfully controlled by treatment of the soil with an insecticide.[346] About 70–99% control may be obtained by treating the corn plants with 0.02% rotenone sprays or 1% rotenone dusts.[2, 19, 433] Dusts containing fixed nicotine have given 90% control.[2] Recently a 50% ryania dust applied at 35 lb/acre has proved much more effective than nicotine or rotenone.[23] DDT also is highly effective, 3% dusts proving superior to nico-

tine or rotenone and giving about 90% control, while 10% dusts could give 99% control if residues were not a problem. Suspension sprays containing 0.04% DDT gave about 95% control, and concentrated sprays in oil solution applied from aircraft gave up to 100% control.[19] At a dosage level of 1.5 lb/acre of DDT, results were as good when applied in oil at 3 gal/acre as in water at 50 gal/acre.[21a] Whereas ryania is the most effective dust treatment for the corn borer [216] and involves no consumer hazard, it is expensive; on the other hand, DDT is comparatively cheap and effective, and at normal applications the residue on the kernels within the sheath is within the limit tolerated. Present recommendations for sprays for ground application include 0.15% DDT, 0.5% ryania, and 0.1% rotenone suspensions,[442] although rotenone is not as effective as DDT or ryania.

TABLE 8. Control of Populations of the European Corn Borer (*Pyrausta nubilalis*) in Ears of Sweet Corn [107a]

Insecticide	Pounds per 100 gal	Per Cent Reduction: Direct	Per Cent Reduction: Residual
EPN	0.75	57	79
Heptachlor	1.0	70	77
Aldrin	0.75	70	74
DFDT	1.0	64	73
Dieldrin	0.5	78	49
DDT	1.0	54	40
Parathion	0.5	65	18

A number of compounds, new and comparatively untested at the time of writing, may prove to be superior to DDT. Their direct and residual effects are shown in Table 8. For comparison, the residual reduction with rotenone was only 20%, and with ryania 9%, in these tests; the residual effect was negligible with DDD, methoxychlor, and methyl-DDT, but as much as 56% with dichlorodiphenylnitropropane.[107a] These data were obtained in small-scale tests involving single plants, and in some instances run counter to large-scale tests. For example, heptachlor proved inferior to DDT in aircraft sprays, as also did toxaphene, chlordane, BHC, and methoxychlor.[21,24a,118] Aldrin and DDD proved almost as good, although the latter compound has on occasion proved inferior.[24] Ryania and rotenone are not reliable when

applied in concentrated sprays from aircraft.[24a] Despite its low residual toxicity, parathion applied in 2% dusts has given excellent control.[24]

The melonworm (*Diaphania hyalinata*) was formerly combatted by dusting the foliage of cucurbits with lead arsenate, cryolite, or rotenone.[291] DDT has proved to be immensely superior to rotenone, giving 100% mortality with 0.6% dusts.[433] Thus the melonworm, being an exposed foliage feeder, can be readily controlled with concentrations of DDT that cucurbits will tolerate. But the pickleworm (*D. nitidalis*), which feeds within the fruit, is harder to eliminate. In one test DDT dusts were no better than rotenone, reducing infestations by about 60% only.[19] However, in another series of tests excellent control was achieved with dusts of 3% DDT, 5% DDD, or 0.5% gamma-BHC; only the BHC formulation gave indications of phytotoxicity.[12]

The riceworm, *Nymphula nymphaeata*, which attacks the submerged parts of this semiaquatic crop, may be almost completely controlled in Italy by treating the water with DDT at 0.25 lb/acre, a dosage comparable to that used for killing mosquito larvae. The peach twig borer (*Anarsia lineatella*) has been completely controlled by one application of a 0.04% DDT spray.[19] Promising results were also given by dormant sprays of BHC in oil emulsion.[368] DDT is definitely more toxic than BHC to the greenhouse leaf tier (*Phlyctaenia rubigalis*).[50] This insect was formerly controlled by lead arsenate or pyrethrum,[291] but DDT is now satisfactorily employed.[368] DDT applied in aerosols at a dosage of 5 mg/1000 ft^3 gives excellent control.[386] On the other hand, the sugar-cane borer (*Diatraea saccharalis*) was found to be much less susceptible to DDT than to cryolite,[43] which has been employed for the past two decades. Moreover, DDT encouraged infestations of the yellow aphid to build up. BHC is highly effective against this insect,[43] 1% lindane dusts giving almost 100% control, as also do 10% toxaphene dusts. Ryania dusts proved almost as good as cryolite, but parathion, sabadilla, and chlordane were poor. Toxaphene is more suitable than BHC or cryolite, since it does not allow resurgence of the borer as BHC does, or of the yellow aphid as cryolite is liable

to do.[241] But all the chlorinated hydrocarbons have proved to reduce the ant population and thus favour the increase of the borers.

Other lepidopteran families

Geometrid larvae or "loopers" were formerly controlled by stomach poisoning with 0.4% sprays of lead arsenate. Since they live an exposed existence on foliage, loopers are readily controlled by DDT. Excellent control of the fall cankerworm (*Alsophila pometaria*) has been obtained with 0.1% emulsions of DDT. This treatment now replaces the 0.3% suspensions of lead arsenate used for orchard and shade trees, and the 4 lb/acre applied by aircraft over forests.[291] The hemlock looper (*Lambdina fiscellaria*) has been controlled by oil solutions of DDT, emitted at the rate of 1 lb/acre in oil solution, in the Pacific Northwest. This treatment was almost half as cheap as using lead arsenate and fish oil.[17] Larvae of the winter moth (*Opheroptera brumata*), a pest of apple in Europe, are readily killed by DDT.[435] The eggs, laid on the bark in late autumn, may be destroyed by dormant sprays of tar distillate or the sodium salt of DNOC.

The diamond-back moth (*Plutella maculipennis*), a pest of cabbage and other cruciferous crops, was originally controlled by the arsenicals applied against the cabbage worm. Nicotine sulphate gives better control than either lead or calcium arsenate, but rotenone is ineffective against the older larvae. Reports from the United States,[19] Europe,[75] Canada,[368] and Australia[217, 422] show that 1% dusts or 0.1% sprays of DDT satisfactorily control these underleaf feeders. The potato-tuber moth (*Gnorimoschema operculella*) may be simply controlled by 1% DDT dust,[388] which is superior to the rotenone dusts previously employed.[274] Single spray applications of 0.1% DDD are equally as effective as 0.1% DDT.[228] When this species appears as a tobacco leaf miner it is also readily controlled by DDT.[77] In either case of infestation, BHC is an inferior insecticide. The bean leaf roller (*Urbanus proteus*) was completely killed by a 3% DDT dust, whereas a 1% pyrethrin dust left 4% as survivors.[333] Larvae of the cherry casebearer (*Coleophora pruniella*) are best attacked as they overwinter on the branches, where 5% miscible oil controls about 93%, and DNBP or the

sodium salt of DNOC (e.g. *Elgetol*) will give complete control.[208, 209]

The vine moth (*Clysia ambiguella*) of Europe was formerly controlled by arsenicals and/or nicotine. DDT sprays were found to fulfill the functions of both of these insecticides and reduced the percentage of infested grapes to 5% as against 20% with nicotine.[133] BHC was found to be of no value.[170] The pink bollworm (*Pectinophora gossypiella*) has been extremely difficult to control with chemicals. Cryolite, the best of the inorganics, does not achieve more than 50% control. The best of the organic insecticides is DDT, which gives about 50% control with 2% dust and 90% with a 10% dust.[19] If the latter dust is applied weekly at the rate of 15 lb/acre, up to 95% control can be expected,[16, 21] while a total of 16 lb/acre distributed in six weekly applications gives 60% control and a 15% increase in the cotton yield.[92a] Methoxychlor is equally effective but leads to a greater build-up of aphids,[21] while BHC and ryania are somewhat less effective poisons for the bollworm.[362] Among forest and shade-tree insects, the larch casebearer (*Coleophora laricella*) may be completely controlled as over-wintering larvae by dormant lime-sulphur sprays, and the various species of *Lithocolletis* leaf miners may be killed in the leaves by 0.1% nicotine sulphate sprays.[222]

Aegeriid larvae, being stem borers, are very difficult to control, the problem being to contact them before they have made entry. The squash borer (*Melittia satyriniformis*) was formerly combatted to a certain extent by Bordeaux mixture or lead arsenate sprays. A control of 75% is possible with rotenone dusts,[291] and of 80% with repeated nicotine sprays.[2] Recently 3% DDT dusts have been found to give satisfactory protection,[19, 83] allowing squash to yield twice as much as when 8% calcium arsenate or 1% rotenone dusts were employed.[71] With soil treatments, only lindane is fully effective, dieldrin being partly so, while chlordane and parathion are ineffective.[238] The peach-tree borer (*Aegeria exitiosa*) has been controlled within its burrows at the base of the trunk by PDB applied to the surrounding soil as crystals or as 3–25% emulsions at the dosage of 0.75–1 oz per tree. Ethylene dichloride in emulsions is more suitable for cooler soils, since it is more volatile; it is also more thorough, achieving 98% control

at 2 oz per tree as compared to 94% wth PDB at 0.75 oz per tree. The dosage rate with ethylene dichloride is usually 0.5 0.75 pt of 10% emulsion per tree, which achieves 98 100% control without the phytotoxic hazard associated with PDB.[28] Propylene dichloride is more insecticidal than ethylene dichloride. It has recently been found that the larvae may be controlled by spraying the tree trunks with 0.1% DDT to prevent their entry into the wood, or with 0.03% lindane to kill them after they have entered.[271] Parathion is excellent in this regard, 0.025% sprays having proved superior to 0.4% DDT, while 0.1% chlordane was not as good.[46] The general infestation of *Aegeria* in the orchard may be completely controlled by the schedule of 0.1% DDT sprays when it is applied against the oriental peach moth, since the deposits kill the adult clearwing moths.[433] However, in heavy infestations the trunk treatments with the new organic chemicals are not as dependable as soil treatments with fumigant emulsions.[396a]

The ash borer (*Podosesia syringae*) has been combatted by the use of trunk washes consisting of PDB in cottonseed oil, which is effective provided the larvae have not burrowed too far into the wood. When the burrows have become large and deep, as occurs with the leopard moth (*Zeuzera pyrina*) and the carpenter worms (*Prionoxystus robiniae* and *macmurtrei*), it is necessary to inject a fumigant such as carbon disulphide, ethylene dichloride-carbon tetrachloride mixture, or nicotine; PDB will also serve as a slow fumigant.[222, 291]

Larvae of the psychid moths, known as bagworms, are not susceptible to control by DDT, because of their habit of spinning bulky silken shelters. For instance, populations of the wattle bagworm (*Acanthopsyche junodi*) of South Africa are only about 30% reduced by DDT, whereas similar applications of cryolite give 70% control.[332] The bagworm *Thyridopteryx ephemeraeformis* of eastern North America is the only shade-tree caterpillar of the region which is not controlled by DDT at practical levels of application.[61] Whereas 100% kill may be obtained with 0.6% sprays of lead arsenate, a 0.2% DDT suspension achieves only 64% mortality.[103] BHC is even less effective, but 0.2% toxaphene sprays give 92% control and 0.3% parathion sprays are now recommended for complete control.[146]

Even 0.1% parathion sprays completely controlled *Thyridopteryx* on white cedar without injuring the foliage, whereas 0.1% chlordane sprays proved ineffective.[337a]

Hymenoptera

Although they are chewing insects, sawfly larvae are more susceptible to control by contact insecticides than by stomach poisons. Lead arsenate is unsatisfactory for the plum sawfly (*Hoplocampa flava*), and quassia, nicotine, or rotenone is used. With the currant sawfly (*Nematus ribesii*) in Holland, 0.01% rotenone was found to give a complete kill, which calcium arsenate failed to do. Rotenone or pyrethrum is favoured for this species in North America. DDT was effective in controlling *H. flava* and *H. minuta* on plum but was inferior to the usual nicotine spray in controlling *H. testudinea* on apple in England.[153] Rotenone is preferred to DDT for the control of *H. minuta* and *H. testudinea* in Holland.[38] In Switzerland, either BHC or SPC (polychlorocyclane sulphide) has been found better than DDT to control *Hoplocampa* spp. on pear and plum.[52,170] Rotenone or lead arsenate are usually applied against the raspberry sawfly (*Blennocampa rubi*). The pear slug (*Caliroa limacina*) in Australia has been effectively controlled by either the lead arsenate or the nicotine sulphate in orchard sprays. The leaf-mining sawflies of birch (*Fenusa pumila*) and of elm (*Kaliofenusa ulmi*) may be controlled within the leaves by sprays of 0.1% nicotine sulphate in 0.5% soap solution.[222] The cherry leaf miner (*Profenusa canadensis*) is combatted with 0.4% BHC suspensions; this is more effective than either chlordane or DDT.[267a]

The European pine sawfly (*Diprion pini*) could be completely controlled by rotenone or pyrethrum dusts; rotenone was 3–4 times as effective as pyrethrum, being more stable in the open air, and since it killed more slowly it allowed a greater survival of the parasites of the sawfly.[161] DDT has been found to be a highly effective insecticide for sawflies infecting forest and shade trees. The introduced pine sawfly (*D. frutetorum*), the European spruce sawfly (*Gilpinia hercyniae*), and Leconte's sawfly (*Neodiprion lecontei*) are completely controlled by area dosages of 2 or 3 lb/acre,[134] and the results may be satisfactory at a level of 1 lb/acre of DDT.[19]

The wheat-stem sawfly (*Cephus cinctus*) in the adult stage, the only stage at which it is not protected within the plant, is comparatively resistant to sprays of DDT, chlordane, and the thiocyanates, but is susceptible to lindane, DNOC, pyrethrins, and nicotine. When BHC was applied to the flying adults in the wheatfields of Alberta, steam-generated aerosols gave almost complete kills, whereas thermally generated smokes were inadequate. Larvae of the pigeon horntail (*Tremex columba*) may be fumigated within their burrows in tree trunks with CS_2 or ethylene dichloride-CCl_4 mixture.[222] It has been found that DDT spray applications protect apples, pears, and peaches against surface injury by wasps (*Vespa* spp.).[362a] *Vespula* and *Polistes* may be eliminated in their nests by application of DDT or, still better, by BHC.[131a]

Diptera

Root-infesting anthomyiids such as the onion maggot (*Hylemyia antiqua*) and cabbage maggot (*H. brassicae*) are most effectively controlled by treating the seeds or seedlings with calomel (HgCl).[78,141] However, Bordeaux mixture has frequently been used against the onion maggot, and corrosive sublimate ($HgCl_2$) may be employed against the cabbage maggot.[291] DDT is cheaper than calomel and has proved effective against the onion maggot when applied as a seed treatment[276] or as a seedling drench;[221,304] dusts are useless.[286] The cabbage maggot is more difficult to control with DDT, since sprays, seed treatments, or diluted dusts are ineffective,[19] only 25% dusts giving control on radishes.[53] Application of a 5% DDT emulsion to cabbage seedlings when they were set out was found to give lasting protection against *H. brassicae* and *H. floralis*.[433] BHC, chlordane,[410] or toxaphene is considerably more toxic than DDT, DDD, or $HgCl_2$ to the cabbage maggot; methoxychlor, HETP, pyrethrins, ryania, and sabadilla showed little or no toxicity.[123] Almost complete control may be obtained by applying 27.5 lb/acre of BHC (10% gamma) to the soil and mixing it to a depth of 8 in. to give a concentration of 1 lb/1000 ft³. Other soil insecticides, including chlordane, toxaphene, DDT, and propylene dichloride, were ineffective against *H. brassicae* when applied in this way.[167] Benzene hexachloride has proved very effective

against both *H. antiqua*[286] and the seed-corn maggot *H. cilicrura*,[198] but it is too phytotoxic for seed treatment.[286] Beans may be protected against *H. cilicrura* by soil treatments of BHC or chlordane, but not by DDT or toxaphene;[157a] unfortunately the two effective compounds may taint the bean crop.[360] Recently, dieldrin has proved an excellent insecticide for the onion maggot, and aldrin for the cabbage maggot, although they may present residue hazards.

The carrot rust fly, *Psila rosae*, has been controlled by treating the seeds with calomel or by dusting the seedlings with naphthalene or rotenone.[291] The application of DDT as drenches, sprays, or dusts has given between 70% and 90% control.[433, 443] However, it has been found in British Columbia that neither DDT nor rotenone is as reliable as naphthalene or calomel.[175] BHC dusts containing 0.25% gamma isomer have given complete control under conditions where neither calomel nor DDT gave as much as 50% control.[311]

Fruit-infesting trypetids such as the apple maggot (*Rhagoletis pomonella*) and the cherry fruit fly (*R. cingulata*) have usually been adequately controlled by the conventional spray schedules involving lead arsenate or DDT.[3, 291] Although DDT suspensions have proved more decisive than lead arsenate,[19] they give protection for a shorter period.[114] With DDT the results are apt to be erratic, particularly where dusts are used;[19, 250] it has been found, with *R. cerasi*, that the larger the area treated, the better the chance of good protection on single trees.[433] In eastern Canada it has been found that the DDT schedule must be supplemented by lead arsenate for adequate control of apple maggot.[368] Rotenone, although effective, has not proved superior to the scheduled materials for either species; the same applies to BHC and cryolite.[103] None of the more recent materials, e.g. dieldrin, have proved superior to DDT. It has recently been established that complete control of cherry fruit flies (including *R. cingulata*) may be obtained with 0.04% parathion, a result which neither DDT nor lead arsenate can give.[105] However, from the standpoint of spray residue, it is safest to use rotenone.

There is a group of semitropical fruit flies for which sweetened bait sprays containing tartar emetic were used;[illegible] these are now being replaced by DDT suspensions and more recently by para-

thion. For example, sodium fluosilicate bait sprays first replaced cryolite cover sprays for control of *Pterandrus* in South African orange groves.[355] Then DDT cover sprays were found to give just as good control of *Dacus ferrugineus* in Australian plum orchards as the fluosilicate bait spray. Tartar-emetic bait sprays have been replaced by 0.6% DDT suspensions to control the Mexican fruit fly (*Anastrepha ludens*) in American citrus groves. BHC and chlordane are inferior for control of these flies.[9] In Hawaii, DDT was found to control the melon fly (*D. cucurbitae*) where tartar emetic, rotenone, and nicotine failed, but it involves a phytotoxic hazard to the cucurbits to be protected.[230] Residual sprays of DDT or DCPM were found to protect mangoes against the oriental fruit fly (*D. dorsalis*); methoxychlor and parathion were even more effective.[231] Aldrin and dieldrin are ten times, and lindane and chlordane five times, as effective as DDT in controlling this fly.[84a]

The citrus blackfly, *Aleurocanthus woglumi*, one of the major citrus pests of the world, was formerly controlled with rotenone emulsions, or somewhat less adequately by DDT.[336] Recently, parathion in wettable powders or dusts has proved to be highly toxic to all stages of this fly; DDT gives inadequate control of the immature stages.[337] Aerosols of DDT applied from aircraft gave up to 89% control of the olive fly (*D. oleae*) in Greek olive groves; but it is considered generally inadequate to control this species,[31] while both chlordane and aldrin have shown much more promise in laboratory tests.[201a] The currant fruit fly (*Epochra canadensis*) may be controlled by bait sprays of 0.4% cryolite sweetened with 15% molasses applied at blossom fall, or with 0.1% DDT suspensions.[8]

The leaf-mining agromyzids are occasionally of sufficient importance to demand chemical control. In general, chlordane is more effective than DDT, which had superseded nicotine for control of these insects. Against the French bean fly (*Agromyza phaseoli*), DDT had proved superior to nicotine sulphate[218] and could give control when applied in 1% dusts or 0.1% sprays. Chlordane was very effective against the pea leaf miner (*Liriomyza orbona*), a 5% dust giving 99% control, where similar dusts of DDT or DDD gave only 80% control, BHC 66%, and methoxychlor 40%, with neither rotenone nor lead arsenate proving

satisfactory.[269] For the pepper leaf miner (*L. pusilla*), chlordane-DDT dusts are effective, while BHC-DDT dusts are useless.[284a] To control the aster leaf miner (*L. flaveola*), chlordane, BHC, toxaphene, or parathion has given good results, where nicotine and DDT were inadequate.[246] Benzene hexachloride has given good control of *Phytomyza rufipes* on cabbage and *P. lateralis* on carrot in Switzerland.[198] DDT suspensions have controlled the holly leaf miner (*P. ilicis*), while chlordane proved uncertain.[256a] The rose midge (*Dasyneura rhodophaga*)[368] and the chrysanthemum midge (*Diarthronomyia hypogaea*)[19] may be thoroughly controlled by DDT sprays or aerosols in greenhouses. However, 0.1% DDT sprays have had little effect on the grape-vine gall fly *Lasioptera vitis*.[156] The midge known as the boxwood leaf miner (*Monarthropalpus buxi*) may be completely killed within the mined foliage by 0.2% sprays of DDT, toxaphene, or nicotine, but not by 0.3% BHC sprays.[403]

The tipulid larvae known as leatherjackets (*Tipula* spp.) which infest sod in the British Isles were formerly controlled with emulsions of *o*-dichlorobenzene, which brought them to the surface. They may now be completely controlled by DDT in emulsion at 8 lb/acre or in dusts at 3 lb/acre, or by lindane at 1.4 lb/acre.[111]

Coleoptera

Blister beetles (*Epicauta* spp.), which feed on potatoes and other crops, are hard to control by arsenicals. However, the fluorine poisons, cryolite and barium fluosilicate, in 25% dusts applied at 25 lb/acre, are able to give quick control. Recently, DDT in 3% dusts or 0.02% sprays has been found to give more than 95% kill of *E. lemniscata*.[433]

Larvae of darkling beetles (*Blapstinus* spp.) in California, which previously had been unsuccessfully attacked by spreading cryolite baits on the soil surface, may now be controlled by applying 0.6% lindane or 25% DDT dusts to the soil.[illegible] A 5% DDT dust is sufficient to prevent the depredations of the adult beetles on leafy crops.

The raspberry fruitworm (*Byturus rubi*) in America and the raspberry beetle (*B. tomentosus*) in Europe may be as readily

controlled by DDT as by rotenone, 5% dusts[393] and 0.05-1% DDT sprays giving excellent results.[376] The western raspberry fruitworm (*B. bakeri*) may be controlled by rotenone in 1% dusts or 0.01% sprays, or by 0.1% DDT sprays provided the danger of mite outbreaks is realized.[14]

The Mexican bean beetle (*Epilachna varivestris*) is a coccinellid immigrant to the United States that has proved exceptionally hard to control. Some degree of kill could be obtained with cryolite or rotenone, and basic copper arsenate or phenothiazine was a second-choice alternative.[55] DDT proved to be relatively ineffective, 10% dusts being considerably inferior to derris, and 20% dusts never achieving more than an 80% kill.[154] Concentrated 0.8% sprays and even DDT aerosols allowed the beetles to recover and survive.[133] Methoxychlor was superior to DDT in dusts, but no better than DDT in aerosols.[55,125] BHC is relatively ineffective against this species.[55,315] Chlordane is about equitoxic with DDT,[410] and toxaphene is slightly better;[401] both can control infestations when used in high concentrations.[239] Neither azobenzene nor DNCHP is effective. Sabadilla is no better than DDT, and not as effective as cryolite.[137] Pyrethrum is one of the best insecticides for the Mexican bean beetle, pyrenone dusts being effective,[55] and pyrethrum aerosols being excellent;[125] rotenone aerosols also give a high degree of control. Very good results have also been given by a dust mixture containing 0.45% rotenone, 3% DDT, and 50% sulphur.[55a] The organic phosphates, HETP and parathion, are the most effective synthetic insecticides.[239] Parathion is favoured since it also controls the two-spotted mite, the other important pest of beans. But it must not be applied later than a month before harvest, and the process of application involves some hazard to the operator.[23] Recently, a mixture of dichlorodiphenylnitro-propane and -butane (*Dilan*) has proved highly effective against the bean beetle.

Powder-post beetles (*Lyctus* spp.) in lumber, structural timber, or rustic woodwork may be eliminated by painting the surfaces with a 5% solution of pentachlorophenol in fuel oil or solvent naphtha.[259] The bamboo powder-post beetle (*Dinoderus minutus*) may be combatted by dipping the culms in a 5% DDT solution in kerosene.[333a]

Elaterids

Wireworms infesting soil, such as the larvae of *Limonius californicus*, have been controlled by the liquid fumigants ethylene dibromide and D-D mixture.[268] Special applicators have been developed for soil injection, and improvement in methods has reduced the dosage of D-D necessary from 40–60 gal/acre down to 26–36 gal/acre. The dosage of ethylene dibromide preparations has been reduced from 30–40 gal/acre down to 10–20 gal/acre, corresponding to 36 lb/acre of the pure compound.[407]

Recently investigations have been conducted to determine whether the solid chlorinated hydrocarbons could be substituted, and used at lower dosages without special equipment. DDT achieved 100% mortality of *Agriotes obscurus* at 224 lb/acre[178] and 80% control of *A. mancus* at 25 lb/acre; but at 1 lb/acre it had virtually no effect on *Ludius* spp. On the other hand BHC (10% gamma) gave very good control of *Ludius* at 2 lb/acre.[340] Excellent control of the eastern field wireworm (*Limonius agonus*) and the wheat wireworm (*A. mancus*) has been obtained by discing or harrowing BHC into the soil at the rate of 1 lb/acre of gamma isomer.[330] Potatoes have been completely protected against these species by applying BHC at 0.25 lb/acre of gamma when the field is ploughed.[194] Wireworms in tobacco fields may be controlled by applying BHC at 0.2 lb/acre of lindane along with the fertilizer, and then working it in as the soil is cultivated.[26] Control of *Ctenicera* (*Ludius*) *aereipennis destructor* on the Canadian prairies may be expected at doses of 0.5–1.0 lb/acre of lindane.[30] It has been observed that BHC arrests the wireworm damage to the crop before the larvae are killed, as if it had stopped them from feeding.[138] Chlordane is less effective, requiring 4 times the dosage for the same results as with lindane; heptachlor and aldrin are superior to chlordane.[349] However, both chlordane and BHC are feasible to control the sand wireworm (*Horistonotus uhlerii*) in cotton fields.[21] And the application at 400 lb/acre of 1% chlordane dusts has effectively controlled *Melanotus* and *Conoderus* attacking sugar-cane "seed"; 1% toxaphene dusts were also effective, paralleling 0.2% lindane dusts.[73] Soil treatments of aldrin or dieldrin at 5 lb/acre ade-

quately protect potatoes from wireworms without the risk of taint.

The feasibility of seed treatment with BHC before drilling awaited the production of preparations with a high gamma content, which could be applied in small amounts and involve no hazard to germination. When a sample of lindane was used to treat corn, it gave the seed only moderate protection from the attacks of *Melanotus*. Chlordane was ineffective in this respect, but parathion gave excellent protection without any phytotoxicity.[128] In a recent study, lindane was found to be the most suitable seed treatment for field crops against *Limonius canus* and other species, while aldrin and dieldrin had an extended residual effectiveness.[268a] On the Canadian prairies, a single seed treatment with lindane may disinfest the soil for several years.

Scarabaeids

The larvae of the Japanese beetle (*Popillia japonica*) were originally controlled by soil fumigation with carbon disulphide, or by lead arsenate applied to the surface of the sod at 400–1500 lb/acre. They may be controlled by DDT at 25 lb/acre,[16] a dosage of 10 lb/acre giving the same result as 1000 lb/acre of lead arsenate.[433] BHC, chlordane, aldrin, and parathion are excellent soil insecticides for the Japanese beetle. Chlordane at 10 lb/acre gives over 99.6% kill where DDT at 25 lb/acre gave 91–96% mortality; both chemicals may be applied in dust form by a fertilizer spreader. Chlordane acts much faster than DDT but is less lasting; the dosage required would be less than 10 lb/acre if duration of effectiveness was not also required.[155] Parathion gives even quicker results, 4 lbs/acre giving 99% kill in 5 weeks, as against 88% for chlordane at 8 lb/acre, 68% for toxaphene at 8 lb/acre, and 70% for BHC at 1 lb/acre. In 19 weeks, chlordane had given complete kill, while toxaphene and BHC had left 0.5% surviving.[371] Aldrin was effective at even lower dosages than parathion.[372] For the annual white grub *Cyclocephala*, heptachlor was more effective than aldrin, parathion, or other organic insecticides.[337b] Parathion has no residual toxicity, failing to control *Popillia* a year after an application at 8 lb/acre; whereas DDT at 25 lb/acre was still effective after

$2\frac{1}{2}$ years, and BHC, toxaphene, and chlordane were still good after 18 months.[373]

Chlorinated hydrocarbons may be used to control the adult Japanese beetles as they swarm on vegetation. Crops and orchards may be protected by 5% dusts, 0.04% sprays, or 5% aerosols of DDT, and area infestations on shade trees may be controlled by the application of 1 lb acre of DDT in oil solution.[16] This replaces 0.6% lead arsenate sprays, which are deleterious to the trees, and pyrethrum-rotenone sprays, which are inefficient.[61] When used as 0.1% sprays in orchards and vineyards, BHC or chlordane also gave complete control, but the most lasting protection was given by DDT,[156] suspensions being better in this regard than emulsions.[270] BHC has been found to be repellent as well as toxic.[315]

The appearance of the chlorinated hydrocarbons has made it economically possible to control white grubs in the soil. Kills of *Phyllophaga fusca*, close to the maximum obtainable, result from the application of 10–15 lb acre of DDT or 5–10 lb acre of BHC (15% gamma content). However, DDT is the better of the two materials for sprays to control the adult June beetles in tree foliage.[210] DDT aerosols have been used to kill adult *Phyllophaga* on field crops.[133] Larvae of *Polyphylla perversa* infesting strawberry beds may be eliminated by soil treatment with BHC.[368] Ethylene dibromide in 20% emulsion at 8 gal acre or D-D mixture at 16 gal acre is also highly effective against this species, the former treatment being much cheaper. Larvae of the May beetle (*Melolontha vulgaris*) were formerly controlled in Europe by soil fumigation with CS_2 or PDB.[199] They are now better controlled by BHC than by DDT; BHC is not only repellent, but at 90 lb acre it kills 100% of the larvae as against 76% with DDT.[417] Complete control may be obtained at 60 lb acre of technical BHC, a level which is not at all phytotoxic.[77] Polychlorocyclane sulphide is also better than DDT as a larvicide.[350] Adult May beetles are controlled on foliage by 0.2% suspensions of BHC or DDT; the materials are equally toxic, but the BHC kills more quickly and its toxicity persists for almost as long as that of DDT.[96] When aerial sprays or dusts of DDT were applied to fruit trees in Germany, about 90% kill was achieved initially, and the residues remained repellent for 4–6

days and lethal for 2 weeks.[112] DDT residues render the beetles unable to feed on the treated foliage, but they will leave it to feed on untreated leaves if they are present.[433]

Adult rose chafer beetles (*Macrodactylus subspinosus*) originally required spraying with lead or calcium arsenate or cryolite,[291] but now DDT controls this species in vineyards.[368] The 0.1% DDT suspension is sprayed just before the blossoms open. The adult garden chafer beetles (*Phyllopertha horticola*) of Europe, which withstand poisoning by arsenicals, are killed on apple foliage sprayed with 0.05% DDT suspensions.[433]

The Chinese rose beetle (*Adoretus sinicus*) on green beans in Hawaii, formerly killed only by acid lead arsenate in dosages which were phytotoxic, may be thoroughly controlled by 1% dusts and 0.1% sprays of DDT.[433] The green June beetle (*Cotinis nitida*), infesting tobacco seedling beds, is controlled by 15% fluosilicate baits in wheat middlings; all fluosilicates proved superior to the other inorganics.[6] Soil treatment with parathion at 0.0002 lb/acre has given 90% control, this insecticide being more powerful than aldrin, dieldrin, lindane, chlordane, or toxaphene.[129a]

The white grubs *Anomala* and *Heterodera* in Hawaiian pineapple fields are controlled by soil fumigation with D-D mixture; this material has the advantage of also "rejuvenating" the older tropical soils.[54] *Anomala orientalis* may be completely controlled by addition to the soil of DDT at 50 lb/acre or lindane at 7.5 lb/acre. After 8 months the DDT in the soil still gave 96% control, and the lindane gave 92% control after 19 months.[370] The grubs of the sugar-cane beetle *Lepidoderma* in Queensland, formerly controlled by CS_2, with or without added PDB, are now treated with BHC dusts which are more effective and long-lasting; chlordane is of no value.[22] The dynastine grubs of New South Wales, known as black beetles (*Heteronychus sanctae-helenae*), are controlled either by the application of 6% DDT or 0.5% BHC dusts to the surface of the ground, or by baits of ground maize containing 0.04% gamma-BHC.[420] In New Zealand, the grass grub *Odontria* is controlled by fumigation with D-D, although CS_2, methyl bromide, and chloropicrin are progressively more effective.[244] The Australian pasture cockchafer (*Aphodius howitti*) was completely controlled by DDT at 3

lb acre applied in a 2% dust; the effect persisted for at least a year.[82]

Cerambycids and buprestids

The round-headed borers or cerambycids, which infest weakened trees or logs, have been combatted by spraying the bark with insecticides to prevent oviposition, kill the eggs, or fumigate the young larvae. For the locust borer (*Cyllene robiniae*), either an 8% ODB emulsion or 12% PDB in 30% miscible pine-tar oil has been used.[222] Recently 2% DDT emulsions have proved effective by killing the adults as they oviposit.[431] Pine logs may be protected from long-horned beetles (*Monochamus* spp.) on the skidways by application of 5% DDT emulsions.[380] The smaller species of cerambycids infesting the trunks and limbs of trees have been attacked with dormant sprays consisting of 1 part PDB, 5 parts soluble pine-tar oil, and 5 parts water.[222] Larvae of round-headed borers in rustic woodwork may be killed by painting the surface with a 5% solution of pentachlorophenol in fuel oil. Infestations of the round-headed apple-tree borer (*Saperda candida*) may be prevented by applying a suspension of white lead in linseed oil, or may be eradicated by painting a solution of calcium cyanide in linseed oil.[331] The flat-headed borer (*Chrysobothris femorata*) may be controlled by spraying a solution of PDB in cottonseed oil or painting a suspension of naphthalene crystals in a concentrated soap solution.[222]

Many attempts have been made to control the bronze birch borer (*Agrilus anxius*) by injecting chemicals into the tree trunks. Despite initial reports of favourable results with aloes, negative control was obtained by injecting aloin, thymol, acid fuchsin, nicotine, strychnine, or arsenious oxide.[244a, 370b] An attempt to control the locust borer by injecting potassium cyanide had no effect on the borer but killed many of the trees.[156a]

Chrysomelids

The control of leaf beetles, flea-beetles, cucumber beetles, and asparagus beetles was formerly undertaken with inorganic stomach poisons such as lead arsenate, Paris green, cryolite, and basic copper arsenate. Of the botanicals, only rotenone had sufficient residual properties to be effective. Recently the chlorinated

hydrocarbon insecticides have proved highly effective, since they are extremely persistent and are capable of contact poisoning a well as stomach toxicity. For beetles of this family, DDT has generally proved itself to be a highly effective insecticide; in some cases other chlorinated hydrocarbons are superior.

The Colorado potato beetle (*Leptinotarsa decemlineata*), as it spread eastward from the Rocky Mountains, has been controlled since 1865 by Paris green applied in 0.4% suspensions with added lime. Later it was treated with 0.6% suspensions of lead or calcium arsenate, and still later with cryolite, barium fluosilicate, or rotenone. Its introduction into Europe was followed by the discovery in Switzerland in 1939 that both larvae and adults could be destroyed by DDT.[433] A 4% DDT dust is approximately as effective as a 30% calcium arsenate dust. Although indeed DDT is less effective as a stomach poison than calcium arsenate, and less toxic by contact than rotenone to *Leptinotarsa*, it slowly builds up a better degree of control than either of the older insecticides.[200] Now this synthetic insecticide gives entirely satisfactory control of this pest in Europe;[75] and in North America, although applied mainly for flea-beetle and leaf-hopper control, 3% dusts, 0.1% sprays, and 5% aerosols of DDT give satisfactory control.[160, 190] Of the other chlorinated hydrocarbons, BHC is initially superior but its effect is more transitory, and chlordane has been variously assessed as equivalent or inferior to DDT.[410, 262] When, however, the results are assessed by the yield of potatoes, 0.1% sprays of toxaphene or chlordane appear to be no less effective than DDT, and all three chlorinated hydrocarbons are definitely superior to 0.3% calcium arsenate.[298] Aldrin and dieldrin in 0.025% suspensions are as effective as DDT in 0.1% suspensions.[298a]

The strawberry rootworm (*Paria canella*), formerly treated with lead arsenate or rotenone, is now satisfactorily controlled by DDT.[368] DDT has completely eliminated infestations of *Colaspidema atrum* on alfalfa in Spain.[290] Adults of the red turnip beetle (*Entomoscelis americana*) may be controlled by DDT in 0.1% suspensions, 0.05% emulsions, or 3% dusts; 0.75% rotenone dusts are also effective.[29]

The control of the elm leaf beetle (*Galerucella xanthomelaena*), formerly undertaken by 0.6% lead arsenate, is now completely

achieved by 0.1% DDT, which affords a degree of protection carrying through to the following year.[61] DDT sprays, fogs, and dusts fired by an explosive mortar were all equally effective, as also were applications of rotenone, ryania, or BHC.[171] Dusts containing 5% DDT controlled *Galeruca*, a pest of vegetable gardens in northern Italy.[188] The asparagus beetles *Crioceris asparagi* and *C. duodecimpunctata* were formerly attacked by 0.6% sprays of lead arsenate with oil or soap, followed by rotenone dusts or sprays on the growing crop.[291] Now *C. asparagi* is controlled by DDT, to which it is highly susceptible. However, *C. duodecimpunctata* is much more resistant to DDT, requiring 16 times the dosage necessary for its congener.[368]

The potato flea-beetles (*Epitrix cucumeris*, *tuberis*, *fuscula*, and others) of North America are extremely difficult to poison with arsenicals, since they avoid treated foliage and their food intake is low. Calcium arsenate obtained only about 35% control, lead arsenate being even less effective, and neither was as insecticidal as the Bordeaux mixture applied as a fungicide. Cryolite, basic copper arsenate, zinc arsenite, or rotenone is fairly effective. DDT is highly effective, and satisfactory control of flea-beetles may be achieved by the 3% dusts [71] or 0.1% sprays [160] that are now applied to control other potato insects. In Nebraska, DDT was found to be superior to cryolite, zinc arsenite, or basic copper arsenate for all of the eight insect species infesting potato there.[223] In Minnesota, 2.5% DDT dusts applied at 25 lb/acre gave 97–99% reduction of *E. cucumeris*, a result far superior to any hitherto achieved by any insecticidal treatment.[190] In North Carolina, BHC formulations proved to be as effective as DDT formulations. However, in Pennsylvania neither DDT nor BHC was found to be superior to calcium arsenate as dusts, and DDT sprays were inferior to Bordeaux mixture.[65] In New York State, DDT was found to give no better control of *E. cucumeris* than rotenone.[200] The chlorinated hydrocarbons are more effective against potato flea-beetles when applied in suspensions than as emulsions.[116] Methoxychlor, chlordane, and toxaphene are slightly less toxic than DDT.[119] However, toxaphene may give approximately equal control;[325] and chlordane, despite giving slightly inferior control to that with DDT, may allow greater potato yields.[116] In British Columbia, the addition

of calcium arsenate was found to increase the effectiveness of DDT against the tuber flea-beetle *E. tuberis*,[368] and a combination spray of 0.1% DDT and 0.5% calcium arsenate is recommended.[176] The tobacco flea-beetle (*E. hirtipennis*) is not controlled by cryolite or lead arsenate, rotenone having been the best contact insecticide. Although DDT dusts can kill these beetles, it is considered that where *Protoparce sexta* is also present basic copper arsenate is safest for control of both species.[5] However, *E. hirtipennis* may be 98% controlled by the application of 0.1% DDT sprays at the time of transplanting, while BHC, chlordane, toxaphene, and methoxychlor sprays give 90–95% control.[129]

Sprays and dusts of DDT give good control of cabbage flea-beetles (*Phyllotreta nemorum, undulata, crusciferae, vittata*, and others) in Europe[75, 433] and America.[19] A single application of 5% DDT or 0.25% lindane dust may be found to be sufficient.[19] Chlordane proved to be slightly superior to DDT against *P. vittata*.[410] Flea-beetles on the Canadian prairies (*P. vittata, armoraciae*, and *albionica, Psylliodes punctulata*, and *Systena blanda*) are best controlled by 0.05% DDT sprays at 100 gal/acre or 3% DDT dusts at 35 lb/acre.[41] DDT suspensions or dusts have proved very effective against the flax flea-beetle (*Aphthona euphorbiae*) in Belgium.[75] In Italy, heavy applications of 5% DDT dust gave 80% control of the flea-beetles *Aphthona* and *Longitarsus* and resulted in a 50% increase in yield.[187] The corn flea-beetle (*Chaetocnema pulicaria*) was almost completely controlled by DDT in 0.7% suspensions.[433] The bean leaf beetle (*Cerotoma trifurcata*) is eliminated by the DDT aerosols applied for Mexican-bean-beetle control, and also by pyrethrum, rotenone, or methoxychlor.[125]

The cucumber beetles *Diabrotica melanocephala* (= *vittata*) and *D. duodecimpunctata* are difficult to control by chemicals, since the larvae feed underground and the adults keep to the lower foliage and avoid deposits of poison. Dusts of 10% calcium arsenate, 25% cryolite, or 1% rotenone, or 0.05% nicotine sulphate sprays have been employed. Barium fluosilicate was better than the inorganic dusts mentioned, giving 75% kill against 50–60% for the others.[182] DDT in 3% dusts or 0.1% sprays gives outstanding results, but it usually injures young

cucurbits;[19] BHC is equally good but is considerably more phytotoxic.[63] The southern corn rootworm, another form of *D. duodecimpunctata*, is most effectively combatted by the chlorinated hydrocarbon insecticides. The application of 0.25% suspensions of DDT or BHC to the corn "hills" gives good control in either case, but BHC may be phytotoxic.[165] When dusts were applied to the soil surface before planting, chlordane at 4 lb/acre and lindane at 0.2 lb/acre proved to be the best treatments, closely followed by parathion at 1 lb/acre. Area treatments with 10% dusts of DDT, toxaphene, or methoxychlor give only 80% control.[265] When the spotted cucumber beetle attacks peanuts underground, its depredations may be 85% reduced by DDT applied to the soil at 100 lb/acre, without any injury to the plants. BHC gives equally good control of larvae at this dosage but is decidedly phytotoxic.[192] For sprays directed against the adult *Diabrotica*, BHC is superior to DDT or chlordane, giving 75% control as against 50%, but it is handicapped by its phytotoxicity and its liability to taint the crop.[127] However, a 2% DDT dust can attain 85% control of the beetles.[192] Chlordane, though more toxic in the laboratory, is no more toxic than DDT in the field to either species mentioned above.[410, 421] The northern corn rootworms *D. longicornis* and *D. virgifera* are greatly reduced in numbers by 1 lb/acre of lindane applied at ploughing, 10 lb/acre of DDT being ineffective; the adults are very well controlled by 3% DDT dusts applied at 25 lb/acre.[225]

Bruchids and scolytids

The pea weevil (*Bruchus pisorum*) has been controlled in the field by 0.75% rotenone dusts applied to kill the adult beetles before they oviposit in the peas.[291] In the United States a 5% DDT dust gave slightly better results than the 98% control which could be obtained with rotenone.[19] DDT dusts have proved highly effective against the adult weevils in pea plantings in England[433] and Hungary.[35]

Bark beetles have been formerly controlled by sprays containing PDB or ODB as described above for the control of cerambycids.[222] The elm bark beetles, *Scolytus multistriatus* and *Hylurgopinus rufipes*, vectors of the Dutch elm disease, may be prevented from feeding and breeding by the application of DDT in

0.1% or 0.2% emulsions.[434] It was found that the annual spraying of large elms with DDT at 4 lb per tree reduced the incidence of Dutch elm disease by approximately 80%.[338b] For the protection of cut logs of elm against these species, DDT proved to be inferior to the ODB sprays formerly employed. Residual deposits of DDT have been found to be effective against orchard bark beetles (*S. pruni*) in Europe.[433] Infestations of the mountain pine bark beetle (*Dendroctonus monticolae*) have been controlled by aerial spraying of DDT at 15 lb/acre. In the southern United States, cut logs awaiting transport to the mill may be protected from bark beetles and ambrosia beetles by a 4% solution of BHC (10% gamma) in fuel oil. Sawn lumber may be protected by BHC in emulsion. This insecticide proved to be superior to DDT, toxaphene, methoxychlor, and chloronaphthalene for this purpose.[258] A technique has been developed of injecting living trees with poisons to eliminate broods of *D. frontalis* in shortleaf pine; although this practice kills the trees, it prevents the infestation from spreading through the entire stand.[105a]

Curculionids

The weevils, whose larvae characteristically feed within seeds or on roots, have been exceedingly difficult to control by chemicals. The most effective insecticide formerly developed for the sweet clover weevil (*Sitona cylindricollis*) was barium fluosilicate, which achieved a maximum of 40% control. Now this weevil may be satisfactorily controlled with 3% DDT dusts.[42] Similarly DDT is very effective in sprays and dusts against the pea weevil (*S. lineatus*) of Europe.[75] The clover leaf weevil (*Hypera punctata*), whose larvae were formerly so difficult to poison with insecticides, may now be 90–100% controlled by concentrated sprays of 20% DDT emitted from a blower[311] or by 5% DDT dusts applied at 20 lb/acre.[194] The brown vegetable weevil (*Listroderes obliquus*), infesting lettuce in Australia, is controlled by 1% dusts or 0.1% sprays of DDT.[288] Weevils attacking alfalfa in Spain, of the genera *Phytonomus* and *Apion*, have been completely controlled by DDT applied in sprays at 20 lb/acre or BHC applied in dusts at 9 lb/acre.[4] The species of *Apion* infesting beans in Mexico may be 95% controlled by

0.1% DDT sprays, which are more effective than 0.4% BHC and much more so than 0.2% lead arsenate or 0.6% cryolite sprays.[285] The leaf-eating weevil (*Phyllobius oblongus*) infesting apple foliage in Europe is satisfactorily controlled with DDT sprays.[133] A species of *Phyllobius* infesting cedars and junipers in the United States proved to be susceptible to control by DDT or BHC where lead arsenate had been ineffective.[256]

The white pine weevil (*Pissodes strobi*) is combatted by spraying the terminal twigs, in order to kill the feeding adults before they oviposit. Formerly a 0.4% spray of oleate-coated lead arsenate was employed, but now a 1% DDT emulsion gives thorough control. The pine root-collar weevil (*Hylobius radicis*) is best controlled by spraying the bases of the trees with BHC, which is more effective than DDT, chlordane, or propylene dichloride.[377a]

The other chlorinated hydrocarbons (see Table 9) are also highly effective and have generally proved superior to DDT. Toxaphene is more effective than DDT against the cowpea curculio, both being superior to cryolite, rotenone, ryania, or parathion. Both chlordane and toxaphene are superior to DDT for the alfalfa weevil, although all are very effective. For control of the weevils *Hypera meles*, *Tychius griseus*, and *Sitona hispidula* infesting red clover, the crop yields were greater when DDT was replaced by BHC.[374] And 1% parathion dust applied at 45 lb/acre thoroughly controlled *Tychius* and *Sitona* on alfalfa.[200b] However, the seed yields were greater with DDT than with BHC or parathion when alsike clover was treated to control *Tychius picirostris*. Preblossom applications with 1 lb DDT in 100 gal water per acre reduced the population of this seed-eater by only 20%, but increased the seed yield by 100%.[372a]

TABLE 9. Comparative Effectiveness of Chlorinated Hydrocarbon Insecticides as Dusts to Control Curculionids

Cowpea curculio [431]	*Chalcodermus aeneus*	Toxaphene > DDT > chlordane > BHC
Sweet-potato weevil [99]	*Cylas formicarius*	BHC = toxaphene > DDT
Clover root borer [277]	*Hylastinus obscurus*	BHC > chlordane > DDT
Alfalfa weevil [215]	*Hypera postica*	Chlordane * > toxaphene > DDT
Alfalfa snout beetle [201]	*Brachyrhinus ligustici*	Chlordane > toxaphene > DDT
Tobacco stalk borer [441]	*Trichobaris mucorea*	BHC > chlordane = DDT

* Definitely surpassed by dieldrin (J. Hyman, Feb., 1950).

DDT is definitely inferior as an insecticide to *Hylastinus*, *Cylas*, and *Brachyrhinus* (see Table 9). It has recently been found that dieldrin is the most effective insecticide for *H. obscurus*, followed by BHC and aldrin.[209a] DDT was found ineffective to control the citrus snout beetle (*Sciobius*) from the soil in South Africa, pentachlorophenol being found to be the most suitable insecticide.[256] The root weevils *Brachyrhinus ovatus*, *sulcatus*, *rugoso-striatus*, and *singularis* are best controlled by broadcasting raisin-cereal baits containing 5% sodium fluosilicate.[15] Partial elimination of *B. ligustici* may be obtained with sweetened peanut-shell baits containing this inorganic chemical, but chlordane, toxaphene, or parathion dusts are greatly superior.[291] The Paris green baits formerly used to control *Cylas* adults are far surpassed by dusts containing calcium arsenate, cryolite, BHC, or toxaphene.[99]

The white-fringed beetle, *Pantomorus* (*Graphognathus*) *leucoloma*, which has been recently introduced into Florida to become a general pest of vegetation, has proved difficult to control with inorganic poisons. It has been found that 0.1% sprays of DDT give complete kill of the adults, as against approximately 70% for cryolite or calcium arsenate sprays. DDT showed a contact toxicity which the inorganic poisons lacked.[416] Methoxychlor also gave good results at 2 lb/acre in sprays and BHC (13% gamma) at 0.5 lb/acre in dusts.[15] Larval control may be successfully achieved by treating the soil with 10 lb/acre of DDT, either as a dust or as a suspension, before cultivating, preferably in the fall when the larvae are young or at the surface.* Adult control requires the application of 1 lb/acre of DDT every 2–3 weeks, emulsions being better than suspensions or solutions.[220] Both DDT and cryolite were effective against *P. godmani* on citrus in Australia, while rotenone was fairly effective, and pyrethrum or lead arsenate was valueless.[219]

The boll weevil (*Anthonomus grandis*) is relatively difficult to eliminate, since the larvae are protected within the bolls. The adult weevils have been controlled since 1920 with undiluted dusts of calcium arsenate (40% As_2O_5) applied at 7–10 lb/acre

* Larvae in balled and burlaped plant stock may be fumigated with methyl bromide at 2–6 lb/1000 ft³ [Swank and Latta, *J. Econ. Ent.*, **43**:25–29 (1950)].

from aircraft in the larger fields. About 1940, basic copper arsenate was substituted in regions where sandy soils were being poisoned by the accumulation of calcium arsenate.[47] DDT has proved to be relatively ineffective against the boll weevil,[16,19] 2% dusts giving only 15% kill as against 75% or more with calcium arsenate.[153] However, certain other chlorinated hydrocarbons (BHC, chlordane, and toxaphene) are effective against the adults.[16] Chlordane has the ability to poison the larvae within the bolls or squares, so that the adults die at emergence;[347] BHC can do it almost as well, but toxaphene cannot.[169] When applied as relatively concentrated dusts, 20% toxaphene, 10% DDT, and 3% lindane plus 5% DDT are all equally superior to calcium arsenate;[321] 10% chlordane dusts have been erratic in performance. Toxaphene is recommended to be applied at 2 lb acre (e.g. 20 lb acre of 10% dust) and BHC at 0.3 lb acre of lindane (e.g. 10 lb acre of 3% gamma dust).[21] The susceptibility of the boll weevil to BHC increases with temperature.[58] Parathion is inadequate to control the adult weevils.[275] The approximate toxicity of the chlorinated hydrocarbons and calcium arsenate to eight species of cotton insects is shown in Table 10.

TABLE 10. EFFECT OF INSECTICIDES ON COTTON INSECTS

+ Slightly effective. ++ Moderately effective. +++ Highly effective.
− Ineffective. −− Infestations favoured.

Insect	BHC	Toxaphene	Chlordane	DDT	Calcium Arsenate
Anthonomus	++	++	++	−	++
Aphis	+++	+	+	−−	−−
Nezara	++	++	+	−	−
Psallus	+++	++	+	++	−
Heliothis	−	+	+	++	+
Alabama	++	+	+	−	++

It may be seen that toxaphene is the only insecticide capable of controlling all the destructive species. Sometimes, however, toxaphene induces the appearance of *Tetranychus* infestations; this may be corrected by using sulphur as the dust diluent. BHC is the best insecticide for all species with the exception of *Heliothis;* moreover it lacks residual action. Either calcium arsenate or DDT will remedy these two deficiencies, but BHC

and calcium arsenate are incompatible.[318] Therefore BHC dusts (containing 3% gamma isomer) are combined with 5% DDT. Such mixtures control the cotton aphis twice as effectively as the 2% nicotine in calcium arsenate formerly employed, and can raise the cotton yield by an amount almost twice as great as that obtained with the arsenate-nicotine treatment.[149] Recently, aldrin has proved to be a choice insecticide for control of the boll weevil, and dieldrin is equally effective.*

The apple-blossom weevil (*Anthonomus pomorum*), one of the worst orchard pests of western Europe, has been difficult to control with spray chemicals, and for that reason tree banding has been the principal measure taken. Sprays of DNOC have achieved a measure of control, but the dosage is limited by the hazard of phytotoxicity. Thiocyanates and DNCHP were found to be ineffective, and the most concentrated rotenone preparations achieved only 80% control.[122] It has been discovered that 0.1% DDT sprays give excellent control. Dusts are inferior to sprays, a 5% dust leaving 20% of the blossoms injured ("capped") while a 0.1% spray allows only 4% to be injured. With two or three applications, the number of apples borne on the tree may be more than doubled in English orchards.[153] If the trees are treated just as the buds burst, a single application is sufficient for control.[121] Although they are less effective than DDT,[20] sprays of BHC and DNOC are also used in Europe to combat this weevil.[170]

For the control of *A. piri* in French pear orchards, DDT and phenothiazine were the most effective insecticides: BHC, DNCHP, or pyrethrins proved to be of little value.[49] DDT dusts or sprays control the strawberry-blossom weevil (*A. rubi*) in Holland.[262] For the strawberry weevil (*A. signatus*) in Nova Scotia, 3% DDT dusts or 0.4% sprays were as effective as heavy applications of cryolite; BHC, chlordane, or toxaphene proved to be inferior.[284] However, in New Jersey 1% lindane dusts applied at 40 lb/acre gave almost complete control of the weevil and replaced the lead arsenate-sulphur dusts formerly recommended.[95] For the control of the pecan weevil (*Curculio caryae*)

* Ivy and Scales (*J. Econ. Ent.*, **43**:590-592) and Parencia and Ewing (*loc. cit.*: 593-595) have recently shown that 2.5% dieldrin dusts are superior to the 20% toxaphene dusts recommended for boll-weevil control.

parathion has proved superior to DDT, BHC, chlordane, and lead arsenate.[313a]

The plum curculio (*Conotrachelus nenuphar*) has been very difficult to combat in apple, plum, and peach orchards. The fumigation of overwintering adults by application of dichloroethyl ether to the soil is only partially effective.[89] Lead arsenate sprays have proved satisfactory in some cases.[3] Acid lead arsenate is more insecticidal but more phytotoxic; it has been mixed with safeners and applied to peach foliage with good effect.[402]

However, peach foliage is so sensitive that the arsenicals and cryolite among the inorganics, and toxaphene and HETP among the organics, cause some degree of injury when applied in concentrations sufficient to kill the curculio. Of the non-phytotoxic chlorinated hydrocarbons, DDT unfortunately fails to control the curculio,[19, 113, 368] allowing as much as 36% of fruit injury in cases where lead arsenate was satisfactory.[3] However, a 0.1% spray of BHC (10% gamma) gives effective control;[395] but since it has the effect of delaying the ripening of the peaches, the surface injury and cat-facing may be just as bad as with lead arsenate.[402] BHC sprays containing 0.07% lindane give 95% kill of curculios in the trees, and 0.1% lindane sprays kill 60% of those in the soil.[191] But unfortunately BHC taints the fruit; this taint appears in the canned product even if the fresh fruit is untainted.[382] Toxaphene is effective against the curculio,[396] but its hazard to peach foliage precludes its use. Chlordane is highly effective, four 0.1% sprays reducing fruit damage down to 3%; but it has caused severe defoliation and some bud injury.[237] Parathion is even more effective,[120] five 0.05% sprays giving complete control; but it may curl the leaves and may be highly hazardous to the spraymen. All three insecticides are repellent to the adult weevils, and all kill the larvae entering the fruits.[134] Dieldrin is highly insecticidal to the adult beetles, while aldrin is inferior.[16a] BHC is the most active in poisoning these larvae, and chlordane is the most effective adulticide.[91] Consequently, if grub-less peaches are what is desired, BHC is the best insecticide, although it is unlikely that these peaches will be accepted by the cannery.[134] If the absence of fruit-scarring and cat-facing is the criterion, this insecticide is inferior and the best choice for use on peaches and apples is a 0.1% sus-

pension of chlordane.[115,184] However, if a number of criteria are considered together, the ranking of the insecticides was recently found to be parathion, then aldrin, dieldrin, chlordane, and finally BHC as the least effective.[91a] Moreover, the acaricide EPN is an outstanding poison for the plum curculio.

Acarina

Mites infesting plants present a peculiar problem in control, since their life cycle is so short that there is nearly always a sufficient proportion of the population in the egg stage to survive the unusual insecticides. Meanwhile their predators, whether insects or acarines, lack this reservoir of eggs to refill their depleted ranks. Therefore when the destructive mites hatch from the surviving eggs they find they have escaped from their biological control. This phenomenon appears whenever a persistent insecticide is used that is not also a mite ovicide; DDT is an outstanding example. Although it is an effective poison for nymphs and adults of the two-spotted mite (*Tetranychus bimaculatus*), DDT cannot kill the eggs;[369] thus a percentage of the population survives and in a few weeks of freedom from predators it becomes more abundant than before. However, DDT effectively reduces the populations of the predacious mites of the genus *Typhlodromus*.[368] Whereas 0.1% DDT sprays can completely control the mite *Eriophyes sheldoni* on citrus, they are ineffective against the red spider mite (*Tetranychus telarius*) on beans and encourage the development of an infestation.[217] In the same manner DDT has been found to lead to an increase in populations of *Paratetranychus*, *Tetranychus*, *Bryobia*, and *Phyllocoptes* on orchard, greenhouse, and crop plants. Thus where DDT is used in orchards a new set of chemicals, ovicidal to mites, has to be added to remedy the upset in biotic balance.

Dormant sprays to kill the overwintering eggs have been applied for control of the European red mite (*Paratetranychus pilosus*), although they cannot prevent outbreaks occurring late in the summer.[3] The winter eggs were formerly killed by tar distillates or miscible oils, or prevented from hatching by emulsions of heavy petroleum,[260] lubricating, or dormant oil.[284,403] The efficacy of dormant petroleum oils increases when they are applied closer to the hatching time, giving three-quarters kill in

March and complete kill when applied as the buds are about to open (pre-pink) in late April.[94] DNOC has been added as an ovicide, but it has been denied that this compound can kill winter eggs,[260] and recently its addition to dormant oil has been shown to be useless.[94] However, the addition of DNBP to the oil is very effective, and aqueous solutions also of this dinitro compound have given 95–99% kill of *Paratetranychus* eggs.[208]

The main problem is to find materials which are suitable to control tetranychid mites throughout the summer. Summer oil in 2% emulsions is effective,[255] but it cannot be used with sulphur fungicides or with DDT, because it increases the hazard to foliage.[108] Elemental sulphur, lime-sulphur, potassium sulphide, and thiocyanates have been used as summer miticides.[74, 284, 291, 408, 424] Rotenone and xanthone have prevented serious mite outbreaks.[109] Nicotine gives good control of mites but is not as effective as white oil emulsions.[255]

For the control of *T. telarius* * in the greenhouse, rotenone sprays [448] and naphthalene fumigation have been employed.[291] Because of the difficulty of wetting their foliage by sprays, carnations in greenhouses are protected by treatment of the soil with sodium selenate at 0.5 gm/ft^2, which is absorbed into the sap of the plant; chrysanthemums may be protected likewise.[164] The cyclamen mite (*Tarsonemus pallidus*) has been sprayed with nicotine or rotenone, or fumigated with HCN in the greenhouse, or with methyl bromide when it infests strawberries in the field.[72]

One of the first of the synthetic insecticides to be developed was the dinitro compound DNCHP, certain of whose salts (the ammonium, ethanolamine, triethanolamine, and dicyclohexylamine) are quite safe to use on foliage. The dicyclohexylamine salt (marketed as *DN-111*) gave 98% control of *T. telarius*, as against 66% with lime-sulphur and 27% with elemental sulphur; the ammonium salt of DNOC, on the other hand, killed the foliage before the mites.[379] DNCHP salts, although they are not ovicidal, have given good control of the summer generations of mites in orchards.[3, 309] For control of the Pacific mite, the monoethanolamine salt proved to be more effective than *DN-111*.

* There is good evidence that *T. bimaculatus* and *T. telarius* are the same species (H. H. J. Nesbitt, address to 87th Ann. Meeting Ent. Soc. Ontario, 1950).

whose performance was erratic; DNCHP itself at the higher concentration of 0.03% was almost as effective as its monoethanolamine salt. Against other mites, for example the spruce mite (*P. ununguis*), 0.01% suspensions of *DN-111* have given over 99% control.[306] But the performance of DNCHP has been generally erratic, low temperatures decreasing its effectiveness,[368] and newer miticides have relegated it to the second rank. The dinitro material *Arathane* is an effective acaricide, but its residual effect is inferior.[28a]

Azobenzene has been developed as a miticide for greenhouse application and has proved outstanding for the control of *T. bimaculatus* on lima beans.[239] It is successful in controlling the false spider mite (*Brevipalpus*), which is resistant to parathion.[203] Flavan (2′-hydroxypentamethylflavan), when added as 0.1% suspensions to the late-season DDT orchard sprays, has restricted mite populations to a low level;[13, 323] but this "mite-killing DDT" has caused foliage injury and undesirable fruit coloration.[109] Toxaphene has given quite good control of orchard mites[309, 368] and *T. bimaculatus*.[239] Chlordane is a poor miticide,[309] and of its more potent analogues only dieldrin is acaricidal.[252a] Dioctyl phthalate, potassium ammonium selenosulphide, *Aramite*, and N-dodecyl-2-thiazolinyl sulphide (*IN-4200*) have shown promise against various species of mites.[28a, 236, 313] The last compound, however, has injured pears[307] and has proved inferior as an additive for DDT orchard sprays.[313]

Two good acaricides have been developed from DDT analogues. They are di-(*p*-chlorophenoxy) methane (DCPM) and di-(*p*-chlorophenyl)-methylcarbinol (DMC). Both are ovicides and have a good residual effect.[369] DCPM (marketed as *Neotran*) has given satisfactory control of the citrus red mite (*P. citri*) where DNCHP had proved inconsistent,[247] and has been very effective against *P. pilosus* in apple orchards.[236] However, it has caused quite severe russetting of apple and pear,[368] and it has failed to be effective against *T. bimaculatus*[378] and the clover mite (*Bryobia praetiosa*)[313] on apple. DMC (marketed as *Dimite*) has given excellent results in the field,[109, 309] but it is at present expensive to manufacture.[368] K-6451 or *p*-chlorophenyl-*p*-chlorobenzenesulphonate (marketed as *C-854*) has proved itself to be an outstanding mite ovicide as far as residual effect is con-

cerned.[28a] It is, however, unable to control aphids and the cyclamen mite.[15a] Another sulphonyl compound, *Genitol 923*, is a moderately effective acaricide.

TABLE 11. ACARICIDES FOR *Tetranychus bimaculatus* REARED FREE OF PREDATORS [438]

Wettable powders applied to soybeans artificially infested. Numbers per plant remaining after 21 days.

Compound	Concentration	Mites	Eggs
Parathion	0.009	7	41
DCPM	0.125	12	58
Toxaphene	0.125	48	296
Chlordane	0.125	174	489
DDT	0.125	231	502
BHC	0.125	269	752

The organic phosphates have shown great promise, being excellent for the control of greenhouse mites. They are also suitable for late-season orchard sprays since, like nicotine, they kill aphids such as *Eriosoma*.[424] HETP and TEPP are excellent acaricides but are not ovicidal.[369] In 0.08% concentration, they have completely controlled *T. bimaculatus* on greenhouse roses [151] and on lima beans,[239] and as 0.5% dusts they offer the best control available for *T. willamettei* on raspberries.[248] HETP sprays (0.15%) have given 99.7% control of *Bryobia* in South Australian apple orchards.[255] However, their lack of ovicidal action and residual effect renders the timing of the sprays too critical for practical orchard use. Nevertheless it was found that the addition of monoethanolamine-DNCHP to TEPP makes an outstanding ovicide for *T. bimaculatus*.[368] In the greenhouse, HETP applied in aerosols at 1 mg/ft^3 failed to control the broad mite (*Hemitarsonemus latus*) and the cyclamen mite (*Tarsonemus pallidus*).[386]

These phosphates have been largely replaced by parathion, which is an excellent acaricide and a powerful ovicide and has appreciable residual action. Concentrations as low as 0.004% have given complete control of *P. pilosus* and *T. bimaculatus* in the greenhouse.[368] Parathion has proved to be the best miticide of all for *P. pilosus*,[236] *T. pacificus*,[309] and *T. bimaculatus* [75] on apples, *T. bimaculatus* on soybeans [438] and lima beans,[239, 251, illegible]

Bryobia on apples,[315] and the peach silver mite (*Vasates cornutus*).[80] Its ovicidal action is profoundly affected by temperature, a 0.03% spray killing only 15% of *T. bimaculatus* eggs at 60° F, whereas at 80° F it killed 98%;[368] so that in the field it is ovicidal only at high temperatures. Its superiority as an acaricide, independent of the effect of any predators or parasites since they were excluded from the experiment, is shown in Table 11. For control of orchard mites (*T. pacificus*, *bimaculatus*, and *schoenei*, and *P. pilosus*), two or three applications of the 15% wettable powder suspended at 0.5 lb 100 gal are sufficient. For control of the red spider (*Septanychus* spp.) on cotton in Texas, parathion dust is no more effective and is less lasting than elemental sulphur. For greenhouse mites, a 0.015% spray completely controls *Tarsonemus pallidus* in one application and *Tetranychus* spp. in two. With the citrus red mite, even 0.025% sprays fail to kill eggs. Oddly enough neither HETP nor parathion sprays are effective to control the false spider-mites *Brevipalpus* and *Tenuipalpus*.[342] Otherwise no species of arthropods occurring in the greenhouse fail to be controlled by parathion[386] applied in aerosols at a concentration of 1 mg ft^3.

However, strains of mites resistant to parathion are appearing, and the residual effect of parathion is weak. Recently an analogue of outstanding residual properties has been discovered in the form of EPN (ethyl *p*-nitrophenyl thionobenzene phosphonate). The residue from a 0.008% spray on bean foliage is sufficiently active after 10 days to kill all *T. bimaculatus* mites placed upon it.[28a] That from 0.15% of K-6451 will give an 80% kill after aging for 29 days.[28b] However, EPN has proved inferior to certain other organic phosphates, and to *C-854*, for long-term residual protection in New York orchards.[93a]

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CHAPTER X

Chemical Control of Insects Affecting Man and Animals

General considerations

The control of insects affecting man and animals has been revolutionized by the appearance of DDT. Although its toxicity in some cases is inferior to that of other insecticides, its lack of odour and skin irritancy makes it eminently acceptable for control of ectoparasites. Against the larvae of mosquitoes and blackflies, and adults of all the important biting flies, it is a peerless insecticide.

In certain cases the acceptability of DDT is reduced by reason of its cumulative toxic hazard to warm-blooded animals. Where the direct spraying of livestock is concerned, the hazard of body-fat and milk contamination suggests the substitution of its relatively non-toxic analogue methoxychlor, which has approximately the same insecticidal power. On the grounds of their complete safety, pyrethrum formulations with synergists have also been favoured. Similarly, for the protection of stored food products by treatment of bags or bins, the liability of DDT to be absorbed into the fats of the food dictates the substitution of the safe pyrenones, which have sufficient residual properties in warehouses where sunlight is not a factor. Although DDT may be safely applied to bodies of water for mosquito or blackfly control, the margin of safety for fish is narrow.

For certain species, the toxicity of DDT is inadequate. An outstanding instance is the Acarina; here BHC is used for livestock treatment against mites and ticks and for area spraying against chiggers. For the control of mites affecting human beings, the odour of BHC preparations dictates the substitution of benzyl benzoate. BHC, or rather the lindane component, is more toxic than DDT to sucking and biting lice. But again its odour eliminates it as a lousicide for human beings and renders it less generally acceptable than DDT for livestock.

DDT is also ineffective against dipterous larvae. Housefly larvae are better controlled with BHC, aldrin, or water-soluble inorganic poisons. Cattle grubs are most effectively controlled by rotenone. The aberrant dipteran *Melophagus* is more susceptible to control by rotenone than by any of the chlorinated hydrocarbons, although the latter are highly effective.

The insecticidal power of DDT is insufficient to control ants. Here chlordane and other chlorinated terpenes take its place for residual and direct control. Again for roach control DDT is significantly inferior to chlordane and to toxaphene; the slight hazard involved in the use of chlorinated hydrocarbons in houses and kitchens favours the substitution of pyrethrum sprays.

Although DDT is an excellent insecticide for protection against clothes moths, its susceptibility to ultimate removal from cloth by repeated washing puts it at a disadvantage with the fast organic impregnants (e.g. the Eulans and Mitins) and processes which render wool indigestible. Although effective too against termites, there are cheaper inorganic (e.g. sodium arsenite) or organic (e.g. pentachlorophenol, trichlorobenzene) substitutes.

It has become clear that, for the control of insects affecting man and animals, the chlorinated hydrocarbons are in no danger of being superseded by the organic phosphates. Recent fatalities resulting from the use of parathion have put this latter group of potent insecticides out of consideration in this context.

Mites

The itch mite (*Sarcoptes scabiei*), the cause of human scabies, has been controlled by ointments containing sulphur, pyrethrins, or β-naphthol.[illegible] DDT is ineffective to control infestations of

these fast-breeding arthropods, saturated solutions in oil failing to kill as much as 50%.[152] Benzyl benzoate, however, gives 99% kills, and 25% emulsions were able to eradicate infestations of *S. s. hominis* in American[200] as in the British armed forces.[231] With the idea of substituting prophylaxis for cure, benzoyl benzoate has also been tried for use as an anti-scabies soap; but it is liable to cause dermatitis, particularly in children. Tetraethyl thiuram monosulphide (*Tetmos*) has proved an effective sarcopticide, and under the name of *Tetmosol* it may be incorporated to the amount of 10% in soaps, which have very little dermatitic effect.[90] BHC is an excellent scabicide and is now widely used for livestock treatment. Cases of hog mange caused by *S. s suis* have been completely controlled by 0.25% suspension sprays of BHC, where benzyl benzoate, DDT, or rotenone was inadequate; the lime-sulphur dips and creosote treatments may now be replaced by BHC sprays.[106] Sarcoptic mange of cattle caused by *S. scabiei* and *Chorioptes bovis* is completely controlled by sprays containing 0.6% BHC (= 0.036% gamma isomer), which, however, do not afford the 8-month protection given by sprays containing 3% wettable sulphur or lime-sulphur.[191] Dips which contained as little as 0.015% lindane have been reported to give an apparently complete cure of chorioptic mange on horses and cattle.[210]

The psoroptic mange of horses and cattle was formerly controlled by lime-sulphur, creolin, nicotine,[153] and even hexachloroethane.[227] *Psoroptes bovis* has been successfully controlled by DDT in some cases, but not in others.[199] DDT has been reported to be effective against the rabbit mite (*P. cuniculi*) and the cat itch mite (*Notoedres cati*).[231] Again, BHC gives excellent control, and infestations of *Notoedres muris* causing rat mange may be eliminated by dips containing 0.01% of the gamma isomer.[210] For demodectic mange of cattle, caused by the follicle mite *Demodex bovis*, control has been obtained by BHC in salves, but not in suspension sprays.[217] Application of DDT as an 8% dust on rat runways does not control the tropical rat mite (*Liponyssus bacoti*) as it does the rat flea; sulphur must be added to the dust in order to obtain acaricidal action.[155]

For chiggers or redbugs, such as *Eutrombicula*, the vector of scrub typhus, protection was given to troops in the southwest

Pacific area by dimethyl phthalate, and later by the benzyl benzoate that had been impregnated into uniforms for protection against scabies. This comparatively scarce chemical could be diluted one-half with dibutyl phthalate without loss of its acaricidal activity.[208] The main requirement of an anti-chigger impregnant is that it can withstand laundering. In this respect, six compounds proved to be superior to benzyl benzoate, including four similar esters, BHC, and benzil; the last compound was the most suitable, withstanding twelve washings without much loss in acaricidal activity [49] (see Table 1). DDT does not kill

TABLE 1. Clothing Impregnants as Acaricides against Chiggers [49]
Per cent protection after laundering

Compound	Washings										
	2	3	4	5	6	7	8	9	10	11	12
Benzil	. . .	. .	100	97	100	100	100	99	97	87	83
2-Thenyl salicylate	. . .	. .	. . .	. . .	100	100	75	87			
Diphenyl carbonate	. . .	. .	. . .	. . .	100	100	99	79			
Phenyl benzoate	. . .	. .	. . .	. . .	100	100	98	0			
2-Thenyl benzoate	. . .	. .	99	100	98	100	92	0			
BHC (12% gamma)	. . .	. .	92	39							
Benzyl benzoate	100	99	0								

chiggers fast enough, and its effectiveness is even slower after laundering.[231] In addition to impregnation, these acaricides may be applied as powders to the person and clothing; under such conditions they have given protection for 3–7 days after application, benzil being slightly superior to diphenyl carbonate and *p*-cresyl benzoate.[48]

The chiggers may be controlled by treatment of the scrub areas which harbour them. In Florida, *E. alfreddugesi* (= *Trombicula*

irritans) is accompanied by *Acariscus masoni*, which in some areas is the only species. The application of benzyl benzoate or diphenyl carbonate in sprays or dusts at 5 lb/acre is inadequate. But chlordane, BHC, or flavan has been found to give excellent results at 2 lb/acre.[205] DDT is less effective, even 10 lb/acre being inadequate, and sulphur must be applied at 60 lb/acre to be satisfactory. At 25 lb/acre, pentachlorophenol and valone give essentially complete control, while *Thanite*, biphenyl, and benzophenone are effective but transitory in action. The most effective material is technical BHC or its lindane component.[133] In Australia, the application of lindane at 1.5 lb/acre resulted in 95–99% control of the grass mite (*Acomatacarus australiensis*) near Sydney.[144]

In the control of the chicken mite (*Dermanyssus gallinae*) many of the materials that give quick kills, such as carbolineum, creosote, pentachlorophenol, and BHC, also flavour the eggs even if their application is restricted to the henhouse.[107] Azobenzene is useful because it is a mite ovicide, and the thiocyanates give quick control. But DDT is much more valuable than these quick-acting insecticides, since persistence of control is what the poultry raiser emphasizes. Treatment of henhouses with 1% DDT suspensions has given complete and lasting control of the chicken mite.[151] Similar results have been given by parathion without accident to the birds.[7a]

Ticks

The cattle tick (*Boophilus annulatus*), a vector of Texas cattle fever, was formerly controlled by arsenical dips applied every 2 weeks and containing 0.2% As_2O_3; but these dips depress the condition of the cattle and may leave skin lesions. It has been found that complete control may also be obtained by 1% DDT sprays (although they are less toxic than arsenic to the engorged females), and the cattle are left in good condition and are appreciably less susceptible to reinfestation.[11] In Queensland, where certain strains of *B. a. microplus* (= *B. australis*) had proved resistant to arsenical dips, 1% DDT sprays or monthly 0.5% DDT dips gave effective control. The Australians avoid complete eradication for fear that the cattle will thus lose their resistance to piroplasmosis.[10] With these species in Mexico, it

was found that both DDT and rotenone sprays left some females alive, but 0.5% BHC sprays could destroy them.[199] In Argentina, double dips with BHC amounting to 0.06% lindane prevented the hatching of eggs, which even arsenicals were unable to do effectively.[10] An area spray with 2 lb/acre of DDT could achieve over 90% control of the immature ticks in grassland-palmetto scrub.[14]

The blue tick (*B. decoloratus*), the vector of piroplasmosis and anaplasmosis of cattle in South Africa, has been controlled by sodium arsenite dips, whose minimum effective concentration was 0.64%; in certain areas even these concentrations do not control the resistant strain which has appeared. Rotenone or nicotine is scarcely effective, and 1% DDT dips give only 60% control. But BHC suspensions and emulsions down to a gamma-isomer content of 0.003% give complete control; the dips and sprays are 20 times as toxic as BHC dusts. The female ticks take an extremely long time to die (9–64 days), but they do not feed or oviposit during that period, nor do the eggs hatch.[234] Cattle ticks in Brazil (*Boophilus annulatus*), which had developed increasing resistance to arsenical dips, are now completely controlled by DDT, BHC, or toxaphene.[125]

The gulf coast tick (*Amblyomma maculatum*) was originally controlled by the application of a smear of pine tar in linseed oil to the ears of the cattle and sheep it infests.[153] A greatly superior ear ointment was composed of 5% DDT in rosin, dibutyl phthalate, and methyl abietate.[187] More recently it has been found that application of a 2% DDT suspension spray over the whole animal gives the best control of this tick.[15] Sprays containing 0.5% BHC suspensions (or 0.06% lindane) applied to cattle give complete control of all stages of the lone star tick (*A. americanum*) and protect the animals for 7–10 days.[184] Infestations of this species on dogs may be controlled with 5% emulsions of DDT, although some ticks may complete their engorgement, and the dog may become quite quickly reinfested.[231] The ticks are completely paralysed by 5% BHC dust, but they require mechanical removal. Area sprays of DDT, chlordane, or toxaphene at 2 lb/acre, or parathion at 0.5 lb/acre, keep the pasture disinfested for about 2 months; BHC is inferior in this regard.[157a] Application of 5% DDT solutions can protect calves from

Hyalomma mauritanicum and the bovine piroplasmosis (*Theileria*) which it transmits, but treatment must be repeated twice weekly.[195] BHC sprays containing 0.1% lindane protect cattle against the sage tick or spotted fever tick (*Dermacentor andersoni*) for 2 weeks.[91] The winter tick (*D. albipictus*) has been controlled on horses by sponging them down with 0.8% DDT emulsions,[2] and 1% emulsions are recommended as standard treatment.[225] The American dog tick, or wood tick (*D. variabilis*), may be controlled on canine pets by dusts, sprays, or baths containing rotenone or DDT. Field populations of wood ticks on Long Island, New York, may be kept down by spraying the margins of roads and paths with DDT at 1–2 lb/acre.[87] Lindane at 1 lb/acre gives excellent control. In Massachusetts, DDT at 1 lb/acre controls *A. americanum* and the black-legged tick (*Ixodes scapularis*), but 2.5 lb/acre is required for satisfactory control of *D. variabilis*.[91]

The brown dog tick (*Rhipicephalus sanguineus*) has been completely controlled by washing dogs in 2% DDT emulsions, or by dusting them with 10% DDT in pyrophyllite. However, some female ticks may survive to oviposit; and the dog may become reinfested unless his habitation is also treated.[231] Even 5% DDT solutions, a concentration too hazardous to be practical, kept the dogs free of ticks for only 1 week.[195] The east coast fever tick (*R. appendiculatus*), which infests cattle in Uganda, may be controlled by ear sprays of 5% DDT or enough BHC to give 0.65% lindane; since they are effective for only 4 days, applications must be made twice weekly.[235] Sufficient protection to inhibit transmission of the fever may be attained by administering weekly oral doses of 250 mg/kg of BHC (13% gamma), whereby the ticks are prevented from engorging before the acaricide causes them to detach.[236]

The argasid tick (*Ornithodorus moubata*) is comparatively resistant to DDT.[231] This species may be eliminated in East African dwellings by two heavy applications of BHC at 1.25 gm/ft^2, timed so that all ticks that escaped the first treatment in the egg are killed by the second treatment as they hatch.[105a] The dusting of BHC on the floors is also sufficient to eliminate this human tick that carries relapsing fever.[182a] The spinose ear

tick (*O. megnini*) in Texas and Mexico was somewhat inadequately controlled by 5% DDT salves applied to the ears of cattle,[231] but BHC in pine oil gives satisfactory control.[199]

Silverfish

These household insects were formerly controlled with pyrethrum, sodium fluoride, or rotenone powders. PDB-CCl_4 sprays as used for clothes moths were also quite effective. Sweetened oatmeal baits containing 8% NaF or As_2O_3 have also been used.[153] It has been found that DDT effectively controls *Lepisma saccharina*.[231] In Australia, the important household pest *Ctenolepisma* may be controlled by 5% DDT dusts.[93] Chlordane is also a highly effective poison for silverfish.

Termites

The best all-round insecticide for termites is pentachlorophenol.* Solutions of it, or of sodium arsenate, are used to destroy termites in their galleries.[237] This material as its Na, Cu, Pb, or Zn salt may be impregnated into wood, where it gives longer protection than the other impregnants used, such as copper sulphate or orthophosphate, zinc chloride, fluoride, or fluosilicate, pyridyl- or phenylmercury, cupric or ferric dimethyldithiocarbonate (*Fermate*), against *Kalotermes* in the West Indies.[238] Copper naphthenate gives remarkably long protection—6 years against *Coptotermes* in Hawaii [180]—and DDT protects for a long time.[238] Pentachlorophenol is also excellent as a soil treatment around wooden structures. One gallon of 5% solution in oil is recommended to protect every 2 linear feet of foundation against *Reticulitermes flavipes* in temperate North America. Sodium arsenite is also used in 10% aqueous solution at the rate of 1 gal/ft, but it is dangerous to animals and plants.[229] However, under hot moist tropical conditions it is more lasting than pentachlorophenol. Lead arsenate, cryolite, sodium fluosilicate, phenothiazine, *o*-dichlorobenzene, and trichlorobenzene are also effective treatments.[124] The last compound is recommended for

* Although lindane or chlordane is more toxic to *Reticulitermes* and is recommended as an additive for pentachlorophenol [Hetrick, *J. Econ. Ent.*, **43**:57–59 (1950)].

general domestic use as an 8% solution in oil but must not be used within the house on account of its odour.[13]

Cockroaches

The cockroaches commonly infesting buildings—the German roach (*Blattella germanica*), the American roach (*Periplaneta americana*), and the oriental roach (*Blatta orientalis*)—were formerly controlled by roach powders containing sodium fluoride, sodium fluosilicate, or pyrethrum; rotenone powders have been used but are inferior. Sprays containing thiocyanates or pyrethrins are effective where there are no "dead spots" in the building. DDT powders have been found to be considerably superior to these materials, giving 100% kill at levels at which sodium fluoride or pyrethrum killed only 60%. A 5% DDT dust applied to barracks[93] or restaurants has given adequate and occasionally complete control of the German roach; 3% dusts are too dilute for satisfactory results, so a 10% dust is preferred.[231] DDT dusts are slow in killing, taking 2 days for knockdown of the American roach; but the addition of 5% of a thiocyanate (e.g. β,β-dithiocyanodiethyl ether) will give knockdown within an hour of the application.[192]

However, DDT is in many ways unsatisfactory. Wall treatments of DDT, as also of toxaphene, applied for fly control are relatively ineffective against cockroaches; but applications of chlordane or lindane at 100 mg/ft² give a high degree of control and prevent reinfestation for 8 weeks. Although DDT aerosols are toxic to roaches, they are unable to achieve the effective control that is possible with chlordane aerosols.[77] Cockroaches require about 1 hr to pick up a lethal dose of DDT, whereas with BHC or chlordane 10–20 min of contact is sufficient.[90] The figures in Table 2 show that chlordane and lindane are roughly 10

TABLE 2. Toxicity of Insecticides to the German Roach

Median lethal deposits, $\mu g/cm^2$

	Roaches Sprayed[25]	Roaches Dusted[167]	Container Dusted[167]
Chlordane	1.7	2.0	0.6
Lindane	2.8	0.8	0.2
DDT	40	15	2.5
NaF	....	130	40

times as toxic as DDT,[25] which in turn is roughly 10 times as toxic as sodium fluoride,[167] to the German roach. Toxaphene is intermediate between DDT and chlordane in toxicity.[176] The American roach is more susceptible to DDT than the German roach is, so that DDT is more toxic to it even than lindane.[119] BHC dusts are effective for roach control, but their odour at present eliminates them from consideration as household insecticides.[93]

Pyrethrin sprays have an immediate effect on cockroaches that the chlorinated hydrocarbons lack, flushing them from their hiding places and rapidly knocking them down. On the basis of active toxicant, pyrethrins are several times as toxic as DDT and as toxic as lindane to *Blattella;* they have outstanding knockdown properties, which DDT lacks entirely and lindane shares in some degree.[149] Moreover the toxicity of pyrethrins may be greatly increased by the addition of synergists; addition of 1.5% piperonylcyclonene to 0.3% pyrethrins, neither of which is concentrated enough to kill alone, makes it possible to achieve 98% mortality of *Periplaneta.*[182] In practical control treatments, sprays containing 0.05% pyrethrins plus 1% piperonyl butoxide, or dusts containing 0.1% pyrethins plus 1% piperonylcyclonene, were found to produce an immediate flush, quick knockdown, and a fast complete kill. However, reinfestation occurred, usually within 2 months.[55] The advantage of these pyrenone formulae is that they involve no health hazard whatsoever. But good residual protection of buildings, particularly those with adjoining premises on either side, is to be obtained only with the chlorinated hydrocarbons.

Ants

The control of ants in houses has been undertaken with sodium fluoride or sodium fluosilicate powders scattered along the routes frequented by them; results obtained by this method are extremely erratic. Or the poison may be incorporated in a sweetened paste and confined in salve tins punched with holes to allow the ants to enter; these ant baits or "traps" generally contain thallium sulphate, tartar emetic, or rotenone. The insecticide is carried back to the nest to poison the larvae. Nests may be fumigated outdoors by carbon disulphide or calcium cyanide, and

indoors by a mixture of ethylene dichloride and carbon tetrachloride.[153] Ants are not particularly susceptible to DDT, but chlordane, aldrin, and parathion are sufficiently toxic to give effective control in sprays.

For example, Pharaoh's ant (*Monomorium pharaonis*) is scarcely affected by 1% DDT sprays, although 5% sprays applied at the heavy dosage of 1000 mg/ft^2 greatly reduced the population.[231] Chlordane has proved to be a most effective insecticide for this species; 2% solutions, emulsions, or dusts will give satisfactory control, acting as a contact poison and fumigant directly on the adult ants themselves, and being devoid of any repellent effect. For the Argentine ant (*Iridomyrmex humilis*) in greenhouses, DDT dusts were quite ineffective,[231] but 2% chlordane dusts or emulsions gave complete control. Carpenter ants (*Camponotus pennsylvanicus*, etc.) are rapidly eradicated by treatment of their galleries and runways with 2% chlordane solutions or emulsions.[7]

Colonies of the red harvester ant (*Pogonomyrmex barbatus*) may be completely destroyed by 3% solutions of chlordane; BHC is also highly toxic but is sufficiently repellent to induce many ants to avoid being poisoned.[23] The little fire ant (*Wasmannia auropunctata*), which attacks pickers in citrus groves, is not controlled by DDT suspensions or dusts,[170] although emulsion sprays and dust barriers placed around the grove are effective;[36] both chlordane and toxaphene can control it,[171] but complete elimination is obtained with 0.05% parathion sprays.[172] For control of the mound ant *Solenopsis saevissima*, a 5% chlordane dust was found to be far superior to DDT, BHC, or toxaphene, although these insecticides were very effective.[136] When applied as 0.3% suspension sprays to turf against the cornfield ant (*Lasius americanus*), chlordane gave about 90% control, BHC 60%, toxaphene 45%, DDT 40%, and methoxychlor only 15% reduction.[119]

Colonies of the Allegheny mound ant (*Formica exsectoides*) are not completely destroyed by DDT dusts or sprays, or by fumigation with PDB, and may continue to be quite active; a ring of sodium fluoride around each mound gives much more satisfactory control.[101a] But the application of 1 oz of chlordane to each mound completely kills the colony within 1 day. The

lawn ant *Lasius niger* may be controlled with DDT applied at 2 gm/yd^2, fully 7 weeks being required for the complete effect. But chlordane applied at 0.5 gm/yd^2 (2 oz/1000 ft^2) gave complete control within 1 week, and reinfestation was entirely prevented for 8 weeks thereafter.[189] Aldrin was found to be even more effective than chlordane against *L. niger* and *F. exsectoides*.[190]

Biting lice

Mallophags of the genus *Damalinia* (= *Bovicola* or *Trichodectes*) which infest livestock are readily controlled by DDT,[231] which has completely replaced treatments with sulphur or creosote, arsenical or nicotine dips, and dust treatments with sodium fluoride or rotenone.[158] Emulsions containing 0.3% DDT are generally employed as dips for the American cattle chewing louse *D. bovis*, although concentrations down to 0.08% have given complete control. Treatment with 10% DDT dusts gives fairly satisfactory control.[159] BHC is even more toxic to this species, complete control being obtained with 1% BHC dusts,[217] 0.02% lindane emulsion dips,[74] or 0.005% lindane emulsion sprays.[210] The cattle biting louse of Europe, *D. scalaris*, is also susceptible to DDT treatments.[231]

The biting louse infesting horses in Europe, *D. pilosum*, is susceptible to DDT, which prevents most of the nits from hatching; two successive dustings kept the horses free of lice for at least 2 months.[231] The horse chewing louse *D. equi* of North America is more susceptible to chlordane than to DDT, especially when applied in the emulsion form.[12]

The biting sheep louse (*D. ovis*) has been completely eradicated from herds comprising 1800 full-fleeced sheep by a single dip in 0.2% DDT emulsion.[175] The goat lice *D. hermsi*, *caprae*, and *limbata* were eliminated by 0.3% DDT emulsions, which destroyed even the hatching eggs, and no reinfestation occurred in a month.[231] A more extensive experiment with 450 goats attained complete control with a 0.25% emulsion, with negligible reinfestation 4 months later.[24] The dog biting louse (*D. canis*) may be readily controlled by two treatments with 5% DDT powder,[227] and by a bath in BHC emulsion containing as little as 0.0025% lindane.[210]

DDT is also an effective insecticide of the mallophags infesting birds. Pigeons have been completely freed of the feather louse (*Columbicola columbae*) by being treated with 10% DDT dusts, but *Falculifer rostratus* was only partially controlled within 3 days of application.[210] The various species of chicken lice (*Lipeurus*, *Goniocetes*, *Menopon*, *Eomenacanthus*, etc.) were formerly controlled by dusts or dips containing sodium fluoride.[153] Dusts containing 4% DDT were found to be just as satisfactory as 33% sodium fluoride and superior to 0.5% nicotine.[231] Control may be achieved by spraying the chickens with 4% DDT wettable powder suspension.[1] In a courageous experiment, poultry were completely freed of *Goniocetes* and *Eomenacanthus* by treating the henhouse with 0.7% parathion spray and dusting the birds with 2% parathion dusts; the birds were swiftly freed of lice and survived unharmed, and their eggs were safe to eat.[70]

Sucking lice

The lice of the order *Anoplura* were somewhat more difficult to control before the advent of powerful contact insecticides. Dips containing creosote, nicotine, or even arsenicals have been used, and also rotenone dusts and summer spray emulsions.[153] The short-nosed sucking louse (*Haematopinus eurysternus*) on cattle has, however, proved as susceptible to control by DDT as the biting lice. It is eradicated by 0.3% DDT emulsion dips,[199] and concentrations down to 0.08% give effective control.[2] BHC in 0.3% suspension dips (containing 0.04% gamma isomer) yields satisfactory results,[74] and 0.1% lindane emulsions inhibit hatching of the sucking-louse eggs and attain complete elimination.[200] The long-nosed sucking louse (*Linognathus vituli*) is more resistant, 0.3% DDT dips allowing a light infestation to survive.[199] This species, together with the capillate louse (*Solenopotes capillatus*), requires double the concentrations of DDT that are sufficient to control *Damalinia* and *Haematopinus*.[2] However, it is susceptible to BHC, being controlled by 0.04% lindane dips[74] and eradicated by 0.08% lindane sprays.[2] The dog sucking louse (*L. setosus*) may be eradicated by BHC emulsion baths containing 0.0025% gamma isomer.[210] All the mobile stages of the hog louse (*H. suis*) are killed by 0.5% DDT emulsion sprays; 0.75% dips kill all which subsequently hatch from eggs.[119] BHC is

effective at lower dosages, lotions containing as little as 0.005% lindane giving good control.[210] The hog louse (*H. adventicius*) is completely controlled by 0.2% emulsions of DDT, DDD, or chlordane,[212] or by dusts containing 1% lindane.[217] DDT is effective against the horse louse (*H. asini*) and the dog louse (*H. piliferus*), 5% powders being sufficient to give permanent control of the latter.[231] The rat louse (*Polyplax spinulosa*) is not controlled by DDT as readily as the rat flea, surviving the treatment of rat runways with 8% dust.[155]

The control of the body louse (*Pediculus humanus corporis*) is best effected by a change of clothes and a bath. Disinfestation of clothing has been carried out by fumigation, the hydrogen cyanide formerly used being replaced by methyl allyl chloride in Britain, trichloroacetonitrile in Germany, and methyl formate in Russia.[231] In the United States methyl bromide is used because it is the most ovicidal of the common fumigants.[127] Fumigation is performed with a dosage of 1 lb/100 ft^3 for 30 min at atmospheric pressure, or for 15 min at a 28-in. vacuum.[211]

Where a change of clothing is impossible, as it often is for soldiers, prisoners, and displaced persons in time of war, antilouse powders are used. In World War I a combination of naphthalene with creosote and iodoform, in the proportions 9:2:2, known as NCI powder, was used to kill both lice and nits.[19] At the outset of World War II, naphthalene and tar acids for knockdown were combined with rotenone for residual protection in the British powder AL63. Organic thiocyanates (the *Lethanes*) were developed as lousicides and ovicides to be sprayed on underwear or impregnated on a pleated belt (the Sherlice belt) worn as a louse trap under the clothing.[10] Lauryl thiocyanate was favoured since *Lethane 384* and *Lethane 60* (see Table 3) had proved to be irritating to skins of Caucasians. The American MYL powder was more efficient; it contained pyrethrum, phenol-S as an antioxidant, N-isobutylundecylenamide as a synergist, and 2,4-dinitroanisole as an ovicide.[31,122] The Russians employed diphenylamine in a louse powder which was the equal of AL63; as a clothing impregnant they used bisethylxanthogen, which was as effective as the thiocyanates without irritating the skin, but had a repulsive odour.[231]

TABLE 3. CONTACT INSECTICIDES FOR THE BODY LOUSE [33,34]

Median lethal concentrations in white oil sprayed at a deposit of 0.36 mg/cm²

Compound	m.l.c., %
DDT	0.3
DDD and methoxychlor	0.9
Lethane 384 *	1.5
Lauryl thiocyanate	5.0
Bisethylxanthogen	6.2
Lethane 60 †	8.1

* β-Butoxy-β′-thiocyanodiethyl ether.
† Thiocyanoethyl laurate.

When DDT appeared, it was tested against lice and found to be highly effective. A 10% dust in pyrophyllite caused cessation of feeding in 3 hr, complete knockdown in 6 hr, and complete kill in 20 hr; it gave thorough protection for 3 weeks. Therefore it was speedily adopted as the United States Army louse powder.[32] When blown into the clothing (while still being worn) of 1400 prisoners of war in North Africa, 77% of whom were infested, the DDT powder achieved complete disinfestation.[209] Its use in the louse-born typhus outbreak at Naples in late 1943, where about 2,500,000 individuals were treated with it, immediately cut the daily incidence of new civilian cases from 60 down to 10, and protected the United States Army so that not a single case of typhus occurred.[231] Subsequently DDT was impregnated into underwear and gave complete protection without involving any skin irritation. Impregnation is performed by dipping the garments into a solution of DDT in white spirit or other volatile solvent, so that it is taken up on the wool or cotton fibres to constitute 1% of the garment weight.[100] This was the British requirement; the Americans preferred a 2% impregnation because it would survive six to eight washings. The underwear may be reimpregnated by soaking in 2% emulsions of DDT [114] or by dry-cleaning in a solvent which contains DDT (see below under clothes moths). Since the loss of DDT from the cloth fibres is due to erosion of the nap during wear or washing, further developments logically include either a fixative to retain the DDT on the surface, or the incorporation of DDT into rayon fibres woven into the garment.

DDT is not ovicidal, and 6 hr are required for knockdown of motile stages, as against 15 min for MYL powder. Between 1942 and 1946, a total of 7019 chemical compounds was tested by the U. S. Bureau of Entomology at Orlando, Florida, and 284 promising lousicides were discovered.[62] Further testing showed that under practical conditions only 4 were more toxic than DDT.[61] Their properties and limitations were as follows: [59]

1. *tert*-Butyl valone (2-pivalyl-1,3-indandione), with a quick knockdown; but it does not withstand laundering and is unsafe on human skin.
2. Lindane (gamma-BHC), over 10 times as toxic as DDT, with a quick knockdown; but it is eliminated by two launderings and most preparations either have or subsequently develop a bad odour.
3. Chlordane, over 10 times as toxic as DDT, and giving quick knockdown; but it withstands laundering less than DDT, and it involves a slight toxic hazard to the wearer.
4. Toxaphene, over twice as toxic as DDT, with the same knockdown speed and similar resistance to laundering; but it too involves a slight toxic hazard to the skin.

Thus DDT maintains its position as the best lousicide in spite of the subsequent examination of thousands of candidate compounds. The best compounds for fast knockdown of adults are indole, valone, *tert*-butyl valone, methyl anthranilate, and octyl thiocyanate. The best nit ovicides are chloromethyl *p*-chlorophenyl sulphone (developed in Germany as *Lauseto-neu*), followed by 2,4-dinitrophenyl propionate, 2-benzylpyridine, 3,4-dichlorobenzyl cyanide, diallyl adipate, diallyl succinate, and diazoaminobenzene.[61]

Although DDT powder is effective also against the head louse (*P. h. capitis*), liquid formulae are preferred since they are not noticeable in the hair. Rotenone has proved effective in 1% creams or 0.5% oils. A mixture of thiocyanoethyl laurate and *n*-butyl carbitol thiocyanate dissolved in white oil (termed *Lethane 384 Special*) has been recommended by the Ministry of Health of the United Kingdom; it is highly insecticidal but may cause dermatitis.[?] Oils containing pyrethrum are highly effective and do not irritate the skin.[223] The latest formula consists of a

1% DDT emulsion in 11% benzyl benzoate as the solvent, with *Tween 80* as the emulsifier and 2% benzocaine added to eliminate irritation and to act as an ovicide. This has been called the NBIN formula, and its benzyl benzoate content makes it effective against scabies also. An improvement is the substitution of ethyl alcohol as the solvent, and omission of the emulsifier (the EEAY formula).[231a] The crab louse (*Phthirus pubis*) has been controlled by emulsions containing lauryl thiocyanate or isobornyl thiocyanate,[38] or by salves containing *Lethane 384 Special*, rotenone, or pyrethrum; the last material is safest for use on the sensitive parts affected. The crab louse may be eradicated by a single application of the NBIN emulsion or by two dustings a week apart with 10% DDT in pyrophyllite or talc.[121]

There remains the enticing possibility of oral ingestion of materials that will protect the taker against attack by lice. This has been demonstrated with *tert*-butyl valone on rabbits at a single dose of 2.5 mg/kg, or daily doses of 0.1 mg per individual. Rabbits have also been treated with lindane at daily doses of 30 mg/kg and rendered poisonous to the yellow-fever mosquito, the argasid tick, and the bedbug.[51]

Bedbugs

Cimex lectularius was formerly controlled in sleeping quarters by fumigating them with hydrogen cyanide, methyl bromide, or ethylene oxide, and even by sulphur dioxide from burning sulphur.[153] Sprays containing rotenone or thiocyanates gave a fair degree of control, and pyrethrum was effective but its persistence did not exceed 9 days. It has been found that DDT sprays, and even dusts, applied to the crevices of buildings and bedding, give excellent control of bedbugs.[224] Suspensions and solutions of 5% DDT showed residual toxicity for nearly 200 days, while 20% sprays gave highly effective protection to dwellings for 11 months; even DDT aerosols gave deposits sufficient to protect for 2 months.[139] Experimental treatment of a village and a town near Moscow, Russia, with a 5% emulsion of DDT at 5 cc/m² gave complete control which persisted for at least 3 months.[1] The use of DDT in metropolitan centres such as New York is fast eliminating bedbugs as a source of pest-control operators'

business.[183] Methoxychlor is equally as effective as DDT and is superior to the other analogues.[36] Toxaphene is less toxic than DDT as a residual deposit, but more toxic by direct contact.[176] Both lindane and *p*-chlorophenyl chloromethyl sulphone are more toxic than DDT to the bedbug, as to the body louse (Table 4).

TABLE 4. Insecticides for Bedbug and Body Louse [34,36]

Median lethal concentrations in white oil spray in per cent

Compound	*Cimex*	*Pediculus*
Lindane	0.05	0.02
Lauseto-neu *	0.2	0.1
DDT	0.5	0.3
Methoxychlor	0.5	0.9
DDD	1.2	0.9
DFDT	5.0	1.4

* *p*-Chlorophenyl chloromethyl sulphone.

BHC wall sprays can completely eliminate Triatomid bugs (vectors of Chagas' disease) from Brazilian huts.[182a] DDT dusts are lethal to *Triatoma* and *Rhodnius*, and the blood of living pigeons may be made lethal to *R. prolixus* by oral administration of DDT at 200 mg/kg.[231]

Fleas

Siphonaptera were formerly controlled by the application of pyrethrum and rotenone dusts and dips to the body, and of pyrethrum, rotenone, or thiocyanate sprays to the habitation. Now dwellings may be readily freed of the human flea (*Pulex irritans*) by 5% DDT dusts or sprays.[231] The oriental rat flea (*Xenopsylla cheopis*) may be controlled by dusting rat runways with 8% DDT;[155] this treatment, along with DDT in clothing, was successful in completely protecting Allied personnel during an outbreak of bubonic plague in Casablanca in 1945.[5] The dog flea (*Ctenocephalus canis*) may be eliminated by dusting dogs with 5% DDT, in addition to cleaning the house with 10% DDT dust applied at 0.5 lb/1000 ft^2 or 5% DDT spray applied at 1 gal/1600 ft^2.[22] The same treatment eliminates the cat flea (*C. felis*) when it infests dogs. A 5% BHC dust will de-flea a dog even more quickly.[156] Owing to the cat's habit of licking

itself, DDT should be replaced by rotenone or pyrethrum powders on this animal.[225] The sticktight flea (*Echidnophaga gallinacea*) may be eliminated from poultry by 10% DDT dusts, and from dogs by 5% DDT dusts.[231]

Mosquitoes

Chemical control of mosquitoes formerly consisted of applying oil to the surface of breeding pools at the rate of 1 pt/250 ft^2, equivalent to a dosage of 25 gal/acre. Suitable larvicidal oils preferably contained aromatic, unsaturated, and phenolic compounds to enhance their toxicity, and were applied to the detriment of vegetation and aquatic birds and animals.[153] Anopheline larvae (but not culicine) were controlled by the application of Paris green in dusts or suspensions at about 1 lb/acre.[218] Small bodies of water could be disinfested by pyrethrum (see Table 5 for comparative costs). Phenothiazine applied as dusts at 0.5–2 lb/acre gave good control of *Anopheles* larvae.[163, 218, 228] PDB and tetrahydronaphthalene, copper cyanide, copper arsenite, and calcium arsenite were good substitutes.[138]

TABLE 5. Larvicides for *Anopheles quadrimaculatus*, Compared on Basis of Cost of Material (1947) [218]

Larvicide Formula	Dosage of Formula	Comparative Cost
Fuel oil or kerosene	30 gal/acre	3.00
Pyrethrum, 0.006% emulsion	55 gal/acre	2.60
Paris green, 10% dust	10 lb/acre	0.35
Calcium arsenite (undiluted)	7 lb/acre	0.35
DDT, 1% solution spray	1 gal/acre	0.16
DDT, 20% solution aerosol	0.05 gal/acre	0.10

The control of mosquito larvae was revolutionized by the appearance of DDT. It is as toxic as pyrethrins, giving complete kills at 0.01 ppm in water. It is 100 times as toxic as Paris green,[52] showing an LD_{50} of 0.0025 ppm against *Anopheles quadrimaculatus*.[53] Complete control of mosquito larvae may be obtained at 0.005 lb/acre in shallow water in the laboratory,[52] at 0.05 lb/acre with efficient ground application in the field,[88, 52] and at 0.5 lb/acre with comparatively inefficient large-scale air application.[88, 102] DDT is usually applied as a 5% solution in

kerosene or fuel oil, 0.5 gal/acre, comprising 0.25 lb/acre DDT, giving almost complete control of mosquito larvae under practical condition of aircraft spraying. This has been demonstrated for *Anopheles* and *Culex* in the southwest Pacific, using Cub planes with 15-yd swaths,[222] and in Canada for *Aedes* larvae, using Dakota planes flying at 200-yd strip intervals. For ground spraying with knapsack compressed-air sprayers, dosages of 0.1–0.2 lb/acre DDT will give 90–100% control of *Aedes* larvae.[147] Dusts and suspensions are inferior to solutions and emulsions for larvicidal work. Solutions are slightly superior to emulsions, allowing an LD_{90} of 25 gm/acre as against 40 gm/acre with emulsions for *A. maculipennis*. The droplet size of the spray is of no importance provided water-surface coverage is attained.[112] Solutions in oil are entirely satisfactory, since the deposited droplets immediately spread to form a film. The spreading pressure of kerosene, insufficient to be measured on a hydrophil balance, may be increased by addition of a wetting agent; kerosene containing 0.5% *Triton B-1956* has a spreading pressure as high as 2.2 dynes/cm.[39] The larvae may be poisoned on rising to contact this film,[39] or enough DDT may reach the aqueous phase as the oil dissolves in the water. Aerosols are quite satisfactory for larviciding despite a tremendous loss by drift; the emission of 0.1 lb/acre from aircraft gives 98% control of *Anopheles*, although only 0.01 lb/acre is deposited on the water; culicines, however, are only partially controlled at this deposit.[103] When application was made from the ground with a steam aerosol generator, almost complete control was obtained at 0.1–0.2 lb/acre against *Anopheles* and *Culex* on Guadalcanal, with a 700-yd effective range;[22] and at 0.3 lb/acre against *Aedes* in Manitoba, with a 400-yd range downwind of the generator.[147]

So far, parathion is the only insecticide that rivals DDT in its toxicity to mosquito larvae.* In laboratory tests it proved several times as toxic to *Aedes* larvae and was able to kill all pupae at 1 ppm concentrations.[83] It gave nearly complete control of *Aedes* spp. in the Hudson Bay area at 0.05 lb/acre, whereas DDT at this dosage killed only 57%, and in Alaska parathion was no less effective than DDT. DDD and methoxychlor are almost as effective as DDT; and DDD controls *Chaoborus astictopus* at

* Except dieldrin, which has a longer residual effect than DDT for *Psorophora* and *Anopheles* control.

0.02 ppm without any hazard whatever to fish.[130a] They are followed in effectiveness by heptachlor > chlordane > toxaphene. BHC is inferior and erratic in performance,[91,147,221] its LD_{50} for *Aedes aegypti* larvae being 0.36 ppm. However, all these chlorinated hydrocarbons are completely effective at dosages within 1 lb/acre.

Most culicid larvae show the same order of susceptibility to DDT. However, a California salt-marsh mosquito, *Aedes squamiger*, is comparatively resistant to DDT larvicides. Both *A. squamiger* and *A. dorsalis* are considerably more susceptible to DDD than to DDT.[18] The larvicidal effectiveness of DDT to *Aedes aegypti* or *Anopheles quadrimaculatus* was found not to vary in various types of water.[5] It gradually disappears in time, presumably because of absorption into vegetation and onto mud. However, the DDT may be applied before the larvae hatch if it is more convenient. Prehatching treatments on breeding areas before they are flooded have given good results against the rice-field mosquito *Psorophora confinnis* in Arkansas and the salt-marsh *Aedes* mosquitoes in New Jersey. In the former case, 2 lb/acre may be broadcast with the fertilizer before the fields are flooded.[109] The same has been done for floodwater *Aedes*, against mountain snow-pool species, and by application over snow for control of northern *Aedes*. Winter control operations in Alaska were no less effective than the usual larviciding kills, being 100% with 0.1 lb/acre applied from ground equipment, and 90% at 0.2 lb/acre applied from aircraft. The loss of DDT over the winter was so negligible that applications in the previous fall were as effective as spring prehatching treatments.[221] However, on bare tundra, where the spring run-off is rapid, the control is reduced by loss of DDT into the rivulets before hatching has commenced. For application over snow, oil solutions are inferior to emulsions and suspensions.[116] For application to water overgrown with vegetation, a solution of DDT in xylene may be impregnated in small pellets of bentonite or enclosed in balls of gelatin (e.g. *Tossits*).

Adult mosquitoes may be controlled by applying DDT to large areas around settlements from aircraft. For aerial sprays, virtually complete control of *Anopheles*[24] or *Aedes*[88] may be obtained with application rates of 0.5 lb/acre. With aerosols from

exhaust generators the dosage required is considerably less. However, a level of 0.1 lb/acre is considered adequate for aircraft spraying, since it gives 90–95% control, and reinfiltration is so large a factor that retreatments are necessary every 7-10 days even when an area as large as 30 sq mi is treated.[16] When 100 sq mi of Alaskan subarctic forest is covered, retreatment is necessary after 2 weeks.[16a] This schedule of weekly treatments with 0.1 lb/acre was effective for control of *Aedes* spp. in Alaska and of *Anopheles farauti* in the New Hebrides.[241] If it is desired to proof an area against subsequent infiltration by adult mosquitoes, a single application of 10–15 lb/acre of DDT is required for adequate residual effect; this gives complete kills even after 15 days and has been found to be still quite highly effective after 46 days against *A. taeniorhynchus* and *sollicitans* settling in the sprayed area.[140] Treatment of a 50-ft barrier strip with DDT at 140 lb/acre almost completely eliminated the adult *An. quadrimaculatus* within the barrier.[135a] For residual deposits on vegetation, suspensions are better than emulsions, and oil solutions are inferior, presumably because they involve a loss of surface deposit by absorption into the foliage. On the other hand, for direct control of flying adults DDT suspensions are the least effective and oil solutions are the most suitable.

The application of fogs containing DDT, emitted from a point source on the ground and carried by the wind, is a very effective method for controlling populations of adult mosquitoes. With the steam aerosol generator (Besler), good kills of salt-marsh *Aedes* in Florida were obtained for a distance of 300 yd downwind in bush and 1 mi in the open when a 10% solution of DDT in oil was emitted at the rate of 15 gal/1000-ft frontage.[20] Good results have been obtained with the thermal aerosol generator (TIFA) in open country, at an average expenditure equivalent to 0.05 lb/acre of DDT.[51a] But mosquito control in forest is difficult; if the wind is light the fog passes over at treetop level and does not penetrate; if the wind is high the fog passes through the forest so fast that the period of exposure is too short; there is a point of compromise at a wind speed of about 8 mi/hr where satisfactory control may be obtained within the forest.

For the immediate destruction of mosquitoes in buildings and tents, space sprays are put up from air atomizers or aerosols

from compressed-gas bombs; the insecticide solution is 0.5% DDT plus 0.03% pyrethrins and is applied at a dosage of 0.33 cc/m^3 (equivalent to 1 oz/3000 ft^3).[138] In unscreened dwellings a residual protection is required to eliminate night-feeding anophelines; in the malaria regions of the world screens are virtually unknown to the bulk of the population. The usual treatment is to spray the walls with 5% DDT solution at 100 mg/ft^2 (equivalent to 1 gm/m^2) of DDT itself, and these deposits are expected to remain effective for about 2 months.[138]

This is a great improvement over the time when only pyrethrum was available; then, for instance, *A. fluviatilis* in India could be controlled only by spraying dwellings every day.[194] The application of DDT every 2 months was found to be superior to the twice-weekly schedule with pyrethrins against *A. culicifacies* in India[193] and against *A. gambiae* on the Gold Coast.[223] The question has been raised whether the DDT deposits are actually contacted by night-visiting adult *A. gambiae*, once the initial repellent effect of the vapour of the kerosene solvent has worn off; and it has been suggested that an apparent reduction in day catches in the houses may not represent the true situation existing at night.[219] Even when they do settle on a DDT surface, the mosquitoes are apt to leave more quickly than usual, which often prevents their taking up a lethal dose.[118] For instance, the treatment of huts in British Guiana with DDT at 100 mg/ft^2 gave a resident population reduction of 99% of *A. darlingi*, but the mosquitoes entered the treated huts to feed at dawn and dusk just as readily as untreated huts; however, a material reduction was effected in the amount of overnight feeding.[214] It has also been established that 95% of the mosquitoes (*A. quadrimaculatus*) leaving treated rooms die within 24 hr.[76] For safety and assurance that a lethal dose is taken up, DDT should be applied in the highest concentration that kerosene can dissolve, and it may be applied at long intervals. Deposits from emulsions are apt to remain toxic for a longer period than those from solutions.[185] Emulsions and suspensions also do not exhibit the repellency characteristic of solutions.[161] The effectiveness of suspensions is at a peak when the particle size is 10–20 μ;[96a] rosin is an effective sticker for wall treatments.

In the southern states of the United States, treatment of unscreened houses with DDT has been found to give 97–98% control of *A. quadrimaculatus*;[57, 123] when the deposits were between 150 and 200 mg/ft^2 the effect persisted sufficiently to give 90% control of the house population in the following year.[57] In Greece, house spraying with DDT proved to give more effective control of *A. maculipennis* than larvicide treatments with Paris green, and the results could be measured by a drop in the malarial spleen index; the duration of the protective period in days was found to be roughly equivalent to the number of centigrams of DDT applied per square metre.[135] In Russia, treatment of the living quarters did not reduce materially the field-breeding population, but if the cowsheds and animal quarters were also treated, the larval population dropped by 95%.[161] Incidentally it is idle to treat the cattle themselves with DDT; it does not kill to any extent the mosquitoes (e.g. *Psorophora*) feeding on them.[232]

For residual treatments of walls, DDT is superior to the other chlorinated hydrocarbons. On the basis of initial kill and longevity of toxicity, the order of effectiveness is: DDT > methoxychlor > methyl-DDT > DDD > DFDT.[179] For *Anopheles quadrimaculatus* and *Aedes aegypti*, the order of residual effectiveness was found to be: DDT > BHC and chlordane > toxaphene. At a deposit of 200 mg/ft^2, DDT continues to give complete kills for a period of 15–36 weeks, as against 4 weeks with BHC or chlordane.[77] Under certain conditions, both DDT and BHC may remain effective for a year, as against a maximum of 3 months with chlordane. Pyrenone deposits also may remain effective for 3 months. On clay walls, which absorb DDT and thus reduce the surface deposit, BHC may be superior to DDT, but chlordane is not.[50] For use in space sprays to kill by direct contact, the ranking is again DDT > BHC and chlordane > toxaphene; but lindane, the gamma isomer of BHC, is 2.5 times as toxic as DDT.[77]

Blackflies and sandflies

DDT is an extremely potent insecticide for the larvae of blackflies (*Simulium* spp.), minuscule concentrations in water causing

them to detach and to wash down the stream, to be killed in the DDT-treated water. It was first found that a concentration of 0.1 ppm of DDT was sufficient to clear streams in Guatemala of *Simulium* for 1000 yd downstream.[67] The same effect was observed on *S. venustum* at Churchill on Hudson Bay, the minimum effective concentration being 0.1 ppm for an exposure of 15 min, shorter exposures requiring higher concentrations and longer exposures allowing lower concentrations to be effective.[108] A large-scale application on the South Saskatchewan River to give slightly over 0.1 ppm for a 30-min exposure period achieved virtually complete elimination of larvae of *S. arcticum* for a distance of the order of 100 mi downstream of this large river; no fish were killed at this concentration.[9] Treatment of rivers at dosages averaging 2–10 ppm completely eliminated larvae of *S. neavei*, the carrier of onchocerciasis, over an area of 65 sq mi in Kenya; naturally there was high mortality of fish also.[75] In Alaska, larvae of *S. venustum* and *vittatum* were effectively controlled by DDT at 0.3–0.7 ppm 15 min. Streams running for a distance of 800 yd through areas treated by DDT at 0.1 lb acre for mosquito control were freed of blackfly larvae for 2.5 mi downstream.[84] There is no evidence of differences in susceptibility between species. DDT is quite ineffective against pupae at the level of larvicidal doses. Methoxychlor and DDD are equitoxic with DDT and are superior to chlordane, toxaphene, BHC, and even lindane.[85] However, lindane can achieve a considerable reduction at 0.2 ppm 15 min, and is toxic to pupae, which DDT is not; toxaphene is considerably inferior.[108] Parathion, aldrin, or dieldrin do not compare favourably with DDT as a blackfly larvicide.[107a]

Application is usually made to the surface of the stream by spraying from ground equipment or aircraft; it is probable that pouring oil solutions from drums is hazardous to fish because the oil is not finely broken up. DDT concentrates of specific gravity greater than 1 have killed large numbers of suckers and other bottom-feeding fish. Dilute solutions sprayed on the surface are completely effective, the DDT finding its way into the water as the surfaces of the oil droplets dissolve; however, the addition of a detergent probably aids mixing. Automatic dispensers have

been designed to deliver at slow rates, or insecticidal cakes* have been prepared with PDB or soap to liberate the DDT gradually.[67, 108]

The adult blackflies have been effectively controlled by DDT oil fogs from the thermal aerosol generator on the ground or from a helicopter.[56] Moderately fine sprays from a vertical boom and nozzle assembly have given excellent kills, and coarse sprays have caused about 70% mortality; but remigration soon restores the populations almost to normal. There is some evidence that *Simulium* and *Culicoides* can survive DDT aerosol fogs under certain conditions,[221] but if the dosage is sufficient fogs from ground applicators are effective.

Sandflies of the genus *Culicoides* are extremely difficult to control in the larval stage, since they breed in damp organic matter in swamps. The Palau gnat (*C. peleliouensis*) is an example, breeding at high-tide mark in brackish marshes; here solutions of DDT are not effective because they do not give coverage, but fine dusts containing 10% DDT can achieve good control when applied at 15 lb acre.[56] The larvae of *Culicoides* were found to be fairly susceptible to BHC, being killed by exposure to 0.2 ppm of lindane for 24 hr.[210] With *C. furens* in Panama it was found that area sprays were useless to reduce the adult population, but treatment of fly screens with 5% DDT in kerosene gave good protection to the interior of buildings, reducing the biting rate indoors from 200 down to less than 10.[220] The biting midge *Culicoides impunctatus* of Scotland is apparently difficult to control with DDT.[119a, 104a]

The advent of DDT, however, allowed the control of adult psychodid sandflies. Spraying houses, walls, and caves with 5% DDT in kerosene gave excellent and long-lasting control of *Phlebotomus* spp. in Peru.[102a] Application of DDT at 100 mg ft² gave sufficient protection against *Phlebotomus pappatasii* and other spp. for the whole season to control the incidence of sandfly fever in Greece and the Levant.[111] Adults of the sandfly *Styloconops albiventris* on Guadalcanal in the southwest Pacific

* Briquettes composed of plaster of Paris and sawdust, soaked in an oil solution of DDT, have been used to protect open wells from mosquito breeding [W. C. D. Lovett, *East Afr. Med. J.*, **24**:196–198 (1947)].

were found to be controlled by aerosols of 10% DDT in oil applied at 7 gal/1000 ft of emission frontage.[21]

Horseflies and deerflies

The larvae of *Chrysops discalis* are killed within 2 days by a concentration of 0.2 ppm of DDT.[83a] Aerial treatment with two applications of DDT at 1 lb/acre has controlled *Tabanus nigrovittatus* in its shoreline breeding grounds. This species may also be rapidly killed by soil application of 0.004% pyrethrum emulsions.[10a] But adult *Tabanus* were not controlled by aerial application of 2 lb/acre of DDT or other chlorinated hydrocarbons,[11e] and 4% DDT emulsions failed to protect cattle from the attentions of *Chrysops discalis.*[83a]

Houseflies and flies plaguing livestock

The control of adult houseflies has been accomplished by finely atomized kerosene sprays containing pyrethrum, which give a remarkably quick knockdown; there is no recovery if the concentration of insecticide is adequate. A similar effect may be given by the synthetic thiocyanates known as *Lethanes* or *Thanite*, which can supplement or replace the comparatively expensive pyrethrins. Or the toxicity of the pyrethrins may be increased by the addition of synergists such as N-isobutylundecylenamide (IN-930), ethylene glycol ether of pinene (DHS activator), the sesamin in sesame oil, piperonyl butoxide or piperonyl-cyclohexenone (-cyclonene). The adjuvant effect described for lubricating oil and other non-volatile oils is entirely attributable to their physical effect in fixing the droplets at a suitable size for contacting the insects. Allethrin is more toxic than natural pyrethrins for *Musca*,[208a] but it does not combine as well with the piperonyl synergists.[208b]

DDT is highly toxic to houseflies, but requires at least 10 min to knock them down. Its great value lies in being combined with pyrethrum to kill those flies which would have recovered from the fast initial knockdown. Where 0.07% pyrethrins were formerly required for knockdown and kill, the addition of 0.1% DDT reduces the pyrethrin requirement to 0.03%. Or 0.1% DDT solutions may be combined with 2% *Lethanes* or *Thanite*. These formulations, dissolved in odourless kerosene, give com-

plete control of flies in "space sprays" when emitted at the rate of 1 cc/m³ from air-blast atomizers.[17] When emitted from aerosol bombs in which the propellent is liquefied "Freon," the formulation usually contains 0.3% pyrethrins and 3% DDT in a non-volatile solvent constituting from 10 to 20% of the compressed liquid. The solvent may consist of a mixture of cyclohexanone with sesame oil or lubricating oil, or certain of the aromatic oils (*Velsicol, A.P.S. 202*) alone.

The synthetic insecticide DDT is remarkable in that it can form a toxic film over surfaces, from which houseflies can pick up a lethal dose through their tarsal pulvilli. It was found that a film containing 25 mg/ft² of DDT continued to kill houseflies for 265 days after application.[131] These DDT residual sprays have no repellent effect, except while certain solvents are evaporating off; if they were repellent, they could not contact to kill. If solutions are used, the DDT may stay in supersaturated solution after the solvent has partially evaporated, until some stimulus sets it to crystallizing.[177,178] This crystallization, resulting in regeneration of toxicity, may be brought about by the movements of the flies themselves. The thin liquid films are not fully contacted by the flies' pulvilli and no uptake occurs, whereas when the deposits are crystalline the flies will break off crystal fragments which become lodged among the hairs of the tarsi and pulvilli. However, in some cases, with some insects, a film composed of droplets will prove more toxic than a crystalline film because it is taken up more readily by the insect.[160] Concentrated solutions of DDT are more effective than dilute ones, even for the same area deposit. Similarly, suspensions of DDT have been found by many workers to be more effective than solutions, and emulsions sometimes are.[17] Therefore suspensions are favoured for interior deposits in barns or simple dwellings, but not on wallpaper and fine walls since they leave a visible residue. Oil solutions when used for total wall coverage have the disadvantage of fire hazard. When applied to surfaces which are exposed to the weather, deposits from suspensions are, however, more short-lived than those from solutions.[71]

DDT residual sprays are applied at rates ranging from 25 to 400 mg/ft² and generally at 100 mg/ft².[131] The recommended coverage for 1 gal ranges from 300 ft² with 2% solution[2] to 1600

ft^2 with 5% solution.[225] The spray should be coarse, although fine enough to avoid drip, or the liquid may be painted on. Treatment of fly screens is better accomplished by painting than spraying, since more material can be made to stick, and larger and more abundant crystals may be obtained. Although the treated walls will remain toxic for several months, with the usual applications a second treatment may be necessary to control the autumnal increase in fly population.[231] If the wall surface is smooth, deposits may persist for a long time; deposits of 70 mg ft^2 remain insecticidal for 18 months on glass, wallpaper, or planed wood. If the surface is uneven or porous the deposits become inactive sooner, except when high dosages are involved. It has been suggested that surfaces be pretreated with a sizing agent before the residual sprays are applied.[104] The most effective pretreating materials are those which render the surface impermeable to the insecticide but are nevertheless wetted by it; the most suitable material is the sodium silicate used for sizing cement.[104] Unsized cement surfaces allowed persistence for only 8 months or less. The inefficacy of DDT or BHC residues on concrete has been frequently observed.[169] The mud walls of native huts rapidly absorb DDT sprayed on them in kerosene solution.[11a] Porous surfaces such as unpainted wood exhibit efflorescence of DDT, the residual toxicity increasing some time after application.[17] Newly painted surfaces absorb DDT solutions, to lower their insecticidal power, and the activity is lost in about 8 months; aqueous suspensions are preferable for painted surfaces.[158]

The application of residual wall sprays in barns effects a reduction of about 95% of the fly population; although the numbers of flies entering may build up during the day, they are killed overnight.[231] The treatment of back-door areas and garbage cans in towns by 5% DDT emulsions at frequent intervals can reduce the fly index by 70–85%; weekly spraying of streets and alleys by 5% DDT solution from mist blowers has reduced the fly index by 95% in a Mississippi town.[206] Aerial spraying with DDT at 0.5 lb acre every month reduced the fly population of Manila to negligible proportions.[95] The aerial spraying of Cairo was effective in eliminating houseflies as an element in a typhoid epidemic.

Other chlorinated hydrocarbons have been compared with DDT for their efficacy in controlling houseflies; these studies are particularly significant in view of the appearance of DDT-resistant races. For space sprays and direct contact effect, DDT is more toxic than its fluorine or bromine analogue[165] and considerably more toxic than toxaphene; chlordane is superior to DDT, while lindane is 6 times as toxic,[77] which would make the usual BHC preparation slightly less toxic than DDT. Heptachlor and aldrin are 5 times, and dieldrin 10 times, as toxic as technical chlordane; but they have no knockdown power.[82] As a residual spray DDT is without a peer, deposits of 50–400 mg/ft^2 giving high kills after 36 weeks, at which time lindane, chlordane, and toxaphene have become ineffective. Both in initial killing power and in lasting toxicity, DDT is superior to its analogues, which are ranked as follows: DDT > methoxychlor > methyl-DDT > DDD > DFDT.[179] It is also superior to the other chlorinated hydrocarbons, the order being: DDT > BHC > chlordane > toxaphene > DDD.[79] Nevertheless it will be found, as is so often the case, that these laboratory differences become almost insignificant in the field. Sprays of DDD,[213] chlordane,[28] BHC,[42] toxaphene, methoxychlor,[156] and DDT all give equally satisfactory results against *Musca domestica* in dairy barns. The pyrenone formulae, which contain pyrethrins with piperonylcyclonene or butoxide as adjuvants, are less effective than the chlorinated hydrocarbons.[79] But their residual toxicity may persist for 11 weeks,[113] and they are unimpeachable on the grounds of health hazard. Parathion is superior to chlordane, but not to DDT, for longevity of residual deposits. The best substitute for DDT in areas where resistant strains occur has been found to be BHC; the suspension sprays should contain 0.25% of the gamma isomer. The other chlorinated hydrocarbons are handicapped in some way or another: chlordane in some cases gives only short-lived control, toxaphene allows quite rapid reinfestation, and DDD or methoxychlor meets with the same racial resistance that rendered DDT unsuitable.[8] However, chlordane has been found to be the most consistently effective substitute in Florida, where DDT is now relatively ineffective.[illegible]

The cattle themselves may be sprayed with DDT. Suspensions are used, since solutions introduce a toxicity hazard and emulsions are not so convenient; the concentration varies from 0.1% to 1% DDT. Cattle spraying is the usual method practised for protection against the hornfly, *Siphona* (*Lyperosia* or *Haematobia*) *irritans*; it is also favoured as a measure against the stablefly (*Stomoxys calcitrans*) since populations of this fly are not materially reduced by residual sprays applied to barns.[156] Regular application of 1% DDT sprays to cattle plagued with *Stomoxys* and some *Siphona* in Illinois barns was found to raise the milk yield by as much as 35%.[28] Treatments in Manitoba increased the milk yield by 25% and calf weights by 20%.[199a] The application of 1.5% DDT sprays at 1 pt per head gives complete control of hornfly for 3 weeks. Application may be made to 40 head at a time in a corral with two men using orchard spray guns at 300-psi pressure.[14] Similarly, cattle in Australia may be protected against the buffalo fly (*S. exigua*) for a period of 2 weeks by 0.5% suspension sprays of DDT.[168] The other chlorinated hydrocarbons—toxaphene, chlordane, DDD, and methoxychlor—have given as good results as DDT against the hornfly, although different workers have rated them in different orders; however, all agree that methoxychlor acts the fastest.[63,126,204] When the toxicity of deposits to the stablefly is investigated, DDT and methoxychlor are foremost for speed of kill and longevity of the toxic deposit, followed by parathion and bromo-DDT, then by toxaphene and chlordane (with its analogues heptachlor and aldrin).[64] To reduce the health hazard of DDT to cattle, the addition of pyrenones to the sprays can lower the DDT requirement for hornflies and stableflies by 75%.[143] The relatively non-toxic methoxychlor and DDD have been found to be no less effective than DDT for hornfly control by direct spraying of cattle.[51a,150] An ingenious method formerly used to reduce hornfly population was to feed cattle phenothiazine at 5 gm/100 lb body weight daily to proof their dung against larvae.[153]

Tsetse-flies (*Glossina palpalis* and other spp.), carriers of the trypanosomes which cause sleeping sickness in Africa, are very susceptible to DDT poisoning by direct contact or by residual contact with the pulvilli. This fly is characterized more by its

mobility than its abundance, comparatively small populations per unit area being sufficient to cause concern. A certain measure of control may be obtained by hanging cloth screens treated with DDT to act as traps at strategic points throughout the bush and jungle.[108b] Or the vegetation may be sprayed at points where the flies congregate; about 98% control may be obtained by spraying 4 times at weekly intervals with DDT at 100 mg/ft^2 or lindane at 11 mg/ft^2.[215] When fly areas are treated with DDT fogs applied by a thermal aerosol generator, about 50% control is obtained. BHC smokes applied from 1-lb canisters arranged so as to give a dosage of 1 oz lindane per acre has given up to 90% control; the range of the smoke from these canisters is about 60 yd in dense bush.[108b] Aerial spraying with DDT has given almost complete control when applied to a block of approximately 100-sq-mi area. The spraying of oxen with 9% DDT solutions twice weekly has been found to kill 90% of the female *G. pallidipes* feeding on them, and to achieve an 80% reduction in the infestation level in the area.[233] It has been found possible to treat calves orally with BHC (13% gamma) at 250 mg/kg weekly and render them toxic to any *Glossina* feeding on them.[236] The trypanosome causing cattle sleeping sickness may be controlled by dosing the animals with the drug antrycide.

Maggots and flies parasitic on livestock

The control of houseflies in the larval stage is a special case, because of their comparative resistance to many contact insecticides. Application of borax or sodium fluosilicate to the surface of the breeding locus (refuse pit, manure pile, latrine) is a simple method of control, since these chemicals are sufficiently water-soluble to be carried in by the rain. DDT is relatively ineffective, because it is only slightly toxic to larvae, and it does become mixed in the medium. The most effective materials are PDB, which volatilizes sufficiently to permeate the medium, and ODB, which can penetrate in the liquid state; they are also ovicidal.[115] Laboratory studies indicate that thiourea, phthalonitrile, BHC, and chlordane are highly toxic to *Musca* larvae[26, 148] (Table 6). Recently, aldrin has proved to be a powerful larvicide for *Musca*. The application of DDT to the surface of the breeding medium,

however, has some value, since it is lethal to the susceptible newly emerging flies, and may either poison or repel the adult flies which visit the treated surfaces.[47,145]

TABLE 6. Toxicity of Insecticides to Housefly Larvae

Median lethal concentrations, ppm; chemical mixed in medium.

Compound	Larval m.l.c.[26]	Larval m.l.c.[143]	Life Cycle m.l.c.*
Chlordane	23		
Lindane	44	. . .	8 †
Thiourea	3900	100	81
Phthalonitrile	320	250	. .
DDT	700	. . .	77
PDB	2800	. . .	. . .
Borax	. . . .	2000	924

* Larval mortality as judged by eventual adult emergence.[148]
† BHC (probably approx. 12% gamma).

For the control of blowfly larvae in carcasses (principally *Cochliomyia macellaria*), the most effective insecticide was found to be PDB, ODB, or *Thanite;* DDT was useful to combat the adult flies visiting to oviposit.[145] When applied to battlefields, an area spray of DDT proved moderately effective, treatment of 2 sq mi on Peleliu in the Pacific with six sprays at 0.2–0.6 lb/acre giving 30–50% control of *Chrysomyia megacephala*. When a single spray was applied at 2 lb/acre on a square-mile area in Texas carrying a heavy population of *Phormia regina* and *Callitroga* spp., the maximum reduction achieved was 68% in the centre of the area, but only 6% on the periphery.[132]

The spraying or dipping of sheep with 0.5% DDT was effective in preventing their infestation by the blowfly *Lucilia sericata* in Britain.[65,137] Spraying with 0.1% lindane suspensions gave 95% control of the wool maggots *Phormia regina* and *Lucilia sericata* in the United States.[217] In Australia, blowfly maggots in sheep (mainly *L. cuprina*) have been eliminated by dressings of boric acid in bentonite, with the addition either of creosote (BTB dressing) or lysol and ODB (BKB dressing).[3] Oviposition or "strike" was prevented in the first place by jetting the breech of the animal with calcium arsenite. Now it has been found that 1% BHC emulsions or solutions may be jetted to pre-

vent either breech or poll strike, being as effective as the arsenical,[196] and that the emulsions may be used as dressings to destroy any maggots already there and to prevent restrike.[197] In the southern United States, wounds of farm animals have been protected against infestation by the screwworm (*Cochliomyia americana*) by the application of crystalline diphenylamine, diphenylene oxide,[174] or nitrophenetole. Benzene may be added to the diphenylamine to give protection against the fleeceworms *P. regina*,[120] *L. sericata*, and *Callitroga macellaria*, or it may be combined with biphenyl as a protective chemical.[188] Now control of fleeceworms may be carried out with BHC, chlordane, or toxaphene, the last compound giving the longest protection (55–80 days); DDT, like chlorophenothioxin and biphenyl, is inferior.[92] BHC is an excellent insecticide for control of *Cochliomyia hominivorax* in open wounds of cattle, and it is quite harmless to the host.[210]

Cattle grubs, which are the larvae of the warble flies *Hypoderma bovis* and *H. lineatum*, have been controlled by the application of rotenone washes to the backs of the animals, and of rotenone ointment to the larval cysts. Recent improvements consist in wholesale spraying of herds, since the purpose is general reduction of the local warble-fly population rather than prevention of damage that has been already done. This is carried out with power sprayers; the results improve as the pressure is increased up to 400 psi, though they decrease at even higher pressures since the droplets are too fine to impinge on the coat. No insecticide has been found to be as effective as rotenone. BHC is effective only in salves, not in suspension sprays. Chlordane gives erratic results,[75] toxaphene is inferior, and methoxychlor is ineffective.[216] DDT can be induced to control warbles if thoroughly rubbed into the skin,[231] a practice which is unlikely to benefit the cow or her milk; as a spray it is ineffective. The control effected by rotenone may be increased by the addition of sulphur.[75] A suspension containing 0.25% rotenone and 10% sulphur, applied as a spray at 2 qt per head, may be expected to achieve 98% control, and has proved superior to scrubbed hand-washes at 1 pt per head or 1% rotenone dusts at 3 oz per head.[207]

Horse bots (*Gastrophilus* spp.) are combatted by washes containing creosote to kill the eggs on the coat, and by administra-

tion of carbon disulphide (2 cc/100 lb body weight) to kill the larvae in the intestinal tract. Unfortunately BHC, which can be given orally with safety, is of little effect against these larvae.[216]

The sheep ked (*Melophagus ovinus*) is comparatively easy to eradicate by the use of chlorinated hydrocarbons or rotenone. In Britain, 0.5% DDT dips have been found to give complete control;[137] in Australia, 0.2% dips[166] and even 0.1% sprays[196] do likewise. In the United States virtually complete control is obtained with emulsions of 0.2% DDT[199] or 0.1% lindane.[217] However, rotenone is more effective, cheaper, and safer than DDT for use on sheep.[117] When lambs were treated, 0.5% rotenone dust gave better control than 5% DDT dust.[112] When used in 0.2% suspensions as dips or sprays, DDT and DDD proved to be consistently inferior to the other chlorinated hydrocarbons—BHC, toxaphene, chlordane, and methoxychlor—although all of them gave almost complete or complete control which lasted for at least 4 months. Rotenone was even better than the chlorinated hydrocarbons, complete control being obtained with 0.005% concentrations.[68]

Clothes moths

Clothing and furnishings containing keratinoid proteins (wool, fur, felt, feathers, etc.) require protection against the webbing clothes moth (*Tineola bisselliella*), the case-making clothes moth (*Tinea pelloniella*), the carpet beetle (*Anthrenus scrophulariae*), the black carpet beetle (*Attagenus piceus*), and other species. Larvae of these species can digest keratin because of the presence in their guts of strong reducing agents which can open the resistant disulphide linkages characteristic of this type of protein.[146]

For protection of clothing and other materials in closed spaces such as drawers, chests, and closets, vapours of PDB, ODB, naphthalene, tetrachloroethane, and hexachloroethane are effective.[151] Naphthalene is the least toxic of these, concentrations of 5 lb/100 ft^3 being required with flakes or 10 lb/100 ft^3 with moth balls. PDB crystals ("dichloricide") are effective at a dosage of 1 lb/100 ft^3, and tetrachloroethane and *ortho*-dichlorobenzene are similar in toxicity.[30] These chlorinated fumigants of low vapour pressure are ineffective for use in warehouses and bulk stores. Cedar oil and camphor, older remedies for

clothes moths, have more psychological value as odours than effectiveness as insecticides.

Anti-moth sprays may consist of PDB and/or naphthalene dissolved as 30% solutions in carbon tetrachloride, which itself is a moth fumigant.[129] Fluorides or silicofluorides, particularly sodium fluosilicate and zinc fluosilicate, are used with wetting agents in aqueous sprays. Oil solutions of pyrethrins, rotenone, or the *Lethane* thiocyanates have also been employed. Recently DDT in 5% emulsions or odourless kerosene solutions has proved very effective. Clothing and baled wool in warehouses may be disinfested by surface sprays of DDT solutions[2] or suspensions, or by aerosols applied by a thermal fog generator.[41]

Woollen clothing and other keratinoid material may be protected by mothproofing the fibres and threads themselves. For felts where colour does not matter, 2,4-dinitro-α-naphthol (Martius yellow) and 3,5-dinitro-*o*-cresol (DNOC) give excellent protection and stay fast in the material.[101] Colourless impregnants for clothing may be provided by the fluorides and silicofluorides; the fluorides NaF, CrF_3, and KHF_2 (*Eulan W Extra*), and the Na, Zn, Li, Mg, and NaAl fluosilicates (the last patented as *Larvex*) have been employed. These compounds allow slight surface feeding to take place.[30] The organic fluosilicates (e.g. the triethanolamine salt) are much more resistant to washing.[101]

Research and development are now turning to organic impregnants for mothproofing. A mixture of oleic acid with quinidine and other quinine alkaloids has been used. Triphenyl dichlorobenzyl phosphonium chloride has been developed under the name *Eulan NK*.[101] The sodium salts of dihydroxytetrachlorotriphenylmethanesulphonic acid (*Eulan N*) and the pentachloro analogue (Eulan CN) are widely employed.[129] Further research has led to the development of the superior impregnant *Mitin FF*, a sulphonic acid derivative of urea, *o*-dichlorobenzene, and *p,p'*-dichlorophenyl ether, which is as fast as good dyes and highly insecticidal.[231] Complexes of protein with pentachlorophenol may be incorporated into the wool, thereby yielding a permanent and odourless impregnant (e.g. the *Mystox* formula).[129] The insecticide DDT is excellent as a mothproofer; usually it is impregnated to 0.1% of the clothing weight, although 0.05% is still completely effective. It remains invisible in the clothing until a concentra-

tion of 0.75% is reached. It may be impregnated from solutions or emulsions, and even from suspensions or dusts. It may be incorporated in the carbon tetrachloride or trichloroethylene used in the continuous-flow dry-cleaning process.[203] Although not strongly adsorbed to wool, DDT does become quite resistant to washing when the residue has been reduced to 0.1%.[59] However, it is not permanent enough, as compared with *Eulan CN* or *Mitin FF*, for use on carpets or upholstery.[6] Although chlordane, toxaphene, and BHC are more toxic (to *Attagenus*) than DDT when impregnated at 0.5% on clothing,[128] DDT gives the best protection since it is the least volatile and the most resistant to washing.

Research also has led to the treatment of the disulphide linkage in wool so that it cannot be opened by the insect's alimentary reducing agents.[155a] An alkyl group may be introduced to give an indigestible bis-thioether cross-linkage, by reducing the cystine linkage with thioglycollic acid or sodium hydrosulphite and then treating with an alkylene dihalide, formaldehyde, or glyoxal:

$$\mathrm{R{-}S{-}S{-}R} \xrightarrow[\text{agent}]{\text{Reducing}} \mathrm{2R{-}S{-}H} \xrightarrow[\text{dihalide}]{\text{Alkylene}} \mathrm{R{-}S{-}(CH_2)_n{-}S{-}R}$$

or the disulphide group may be made indigestible by treatment with an acid salt of an aromatic amine (e.g. *Boconize* process).[129]

Stored-products insects

Stored cereal grains and flour products are attacked by many insects, the most important of which are the granary weevil (*Sitophilus granarius*), rice weevil (*S. oryzae*), confused flour beetle (*Tribolium confusum*), red flour beetle (*T. castaneum*), Mediterranean flour moth and related species (*Ephestia kuehniella, elutella, cautella*, etc.), Indian meal moth (*Plodia interpunctella*), Angoumois grain moth (*Sitotroga cerealella*), saw-toothed grain beetle (*Oryzaephilus surinamensis*), and lesser grain borer (*Rhizopertha dominica*). All these may be destroyed by treatment with fumigants, the more powerful contact insecticides in smoke, fog, or spray form, or desiccating and abrasive dusts.[17]

Hydrogen cyanide is not favoured for grain fumigation, since it lacks penetrating power owing to its being rapidly adsorbed and absorbed into the grain. Carbon disulphide is the most economical fumigant; because of its inflammability, it is pref-

erable to use a 20% mixture in carbon tetrachloride, which is effective at a dosage of 20 lb/1000 ft³. Ethylene dichloride is also effective; when diluted with 25% carbon tetrachloride it is used at 40 lb/1000 ft³ (or 8 lb/100 bu). Methyl bromide is the best fumigant for farm bins and for tight warehouses and is effective at a level of 1 lb/1000 ft³. It is outstanding for bagged materials such as flour, on account of its great penetrating power;[4] at 2 lb/1000 ft³ it can fumigate bagged ground-nuts in freight cars and ships' holds,[157] and it may be used to disinfest empty sacks in barges.[27] When cottonseed is fumigated with methyl bromide at 3 lb/1000 ft³, it is completely disinfested of pink bollworm larvae.[181] Chloropicrin is another powerful and penetrating fumigant, being usually applied at 5 lb/1000 ft³. The effectiveness of these fumigants in bulk grain is limited by the fact that, despite the use of injection rods, their vapour tends to channel.

Less volatile fumigants such as ethylene dibromide and acrylonitrile, admixed with carbon tetrachloride, give excellent control of insects in granaries. Of these, ethylene dibromide is the superior spot fumigant. In boxed products acrylonitrile is effective at 0.25 lb/1000 ft³.[2] For vacuum fumigation to tobacco, acrylonitrile is used at 1.25 lb/1000 ft³, being almost as toxic as hydrogen cyanide and very much more penetrating. Trichloroacetonitrile, the German fumigant, is almost as toxic as acrylonitrile, being used at 2 lb/1000 ft³, as compared with 3–5 lb/1000 ft³ for hydrogen cyanide.[11] Chloroacrylonitrile and trichlorobutyronitrile approach these compounds in toxicity.[46] These low-vapour-pressure compounds are applied as "spot fumigants" by pouring a little of the liquid into crevices in the mill machinery where flour collects. For long-lasting effectiveness, they are surpassed by the very slowly volatile chlorinated aliphatic compounds heptachloropropane and hexachloropropene.[201a]

Excellent protection may be given stored grains used for seed by admixture of the chlorinated hydrocarbon insecticides. The median lethal concentrations in grain for *S. granarius* adults and in flour for *E. kuehniella* and *T. confusum* larvae are shown in Table 7. All types of seeds stored for sowing the next crop may be protected from insects such as *Tribolium*, *Plodia*, and *Sitophilus* by admixture of 2.5% DDT, and their germination is

unimpaired.[69] Infestations of *Sitophilus oryzae* and *Sitotroga cerealella* in seed corn (maize) are almost completely eliminated by adding 1.5 oz/bu of 3% DDT dust.[98] Wheat in food stores may be protected by admixture of 100 ppm of DDT; [242] although this gives only 4–6 ppm in the flour, below the 7-ppm tolerance, the fact that flour is such a staple element in the daily diet does not recommend the adoption of such a treatment. The addition of BHC to wheat is safer, as little as 0.4 ppm lindane applied to the top 6 in. of wheat piles being effective against *S. oryzae* and *Rhizopertha*,[79] but the taint of this product militates against its use. Larvae of *Ephestia*, however, are comparatively resistant to DDT and BHC, those of *Tenebrio* are resistant to BHC, and those of *Trogoderma* are highly resistant to most insecticides.

TABLE 7. Toxicity of Chlorinated Hydrocarbons to Stored-Products Insects [26]

Median lethal concentrations, ppm

	Sitophilus	*Ephestia*	*Tribolium*
DDT	16	860	16
Lindane	0.1	10	3
Chlordane	1.3	36	0.2
Hexachloropropene	450	4	10

The treatment of cotton flour bags or jute sacks with DDT, either before or after the contents have been added, achieves disinfestation of most stored-products insects and prevents subsequent infestation.[111] DDD has been found to be equally as effective as DDT for protection against spider beetles (*Ptinus*).[201] However, the use of DDT involves a residue hazard due to its absorption by the food adjacent to the sack,[38a] as much as 100 ppm being absorbed by fatty and finely divided foodstuffs in the outer 1-in. layer. It has been found that pyrenone formulations containing pyrethrum with a synergist, which are without hazard to the consumer, give effective and quite lasting protection to bagged foods stored in warehouses. The use of sacks predipped in pyrenones ensures protection against *Tribolium* and *Ptinus* for 3 months.[202] The spraying of sacks of flour with 0.8% pyrethrin solutions kills adult *Ephestia*, but it has no effect on the larvae already in the flour.[173]

The safest and most effective way of disinfesting warehouses and flour mills, known at present, is to spray the structure with residual sprays of DDT. General fumigation is an emergency measure, and the infestations return to the original level in 4 months. Treatment of warehouses with DDT solutions gives 99% protection of bagged flour stored in them as against 76% when lindane solutions are used.[201] DDT is effective against *Ptinus* in flour stores and *Mezium* in bakeries.[50] But neither DDT nor BHC shows any appreciable residual toxicity to *Ephestia* larvae. Residual wall treatments with pyrethrum sprays have been found to be surprisingly lasting, deposits in cool dark warehouses remaining toxic to *Ephestia* for as much as 100 days. The situation would have been different had the treatments been exposed to sunlight; a pyrethrin deposit that, after standing 2 days in the dark gave 80% mortality of *Ephestia*, gave only 20% kill after 6-hr exposure to light.

A novel method of proofing grain against insects is the addition of finely divided abrasive powders of mineral oxides or silicates, which sear the cuticle and cause desiccation of the insects.[176a] A search for inexpensive materials showed that finely ground magnesite, silica, anhydrite, phosphate rock, and hydrated lime were effective as desiccating dusts.[182a] However, these dusts reduced the flow properties of the grain,[182a] and magnesium oxide was ineffective to protect seed corn against *Sitophilus* and *Sitotroga*.[99] Admixture of 0.5 ppm into bulk stores, or injection into bagged grain, is both safe and effective as a protective measure.[79,182a] The use of magnesium or aluminum oxide dusts in warehouses gave 80–85% control of spider-beetles as compared with 99% control from DDT sprays.[201] Silica aerogel applied to foodstuffs at 250–500 ppm generally gives complete protection against *Tribolium*, *Sitophilus*, or *Ephestia*, and presents no residue hazard since it acts purely as roughage.[15]

Many insecticides have been used as impregnants for food packages to prevent infestation by stored-product insects. They include rotenone, fixed nicotine, the dinitrobenzenes, and DNOC.[43,66,154] DDT was found to be pre-eminent as a package impregnant.[44] However, fatty foods will take up DDT from the package, soya flour absorbing over 100 ppm in the outer inch. Because of the unacceptability of having insect poisons

in contact with foodstuffs, preference has been given to inorganic ammonium salts, which are gustatory repellents, and of which the most suitable is ammonium chloride.[73]

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CHAPTER XI

Insecticides and the Balance of Animal Populations

INTRODUCTION

Man's existence in any area on the earth sets him at conflict with the existing animal population, particularly the arthropods. The colonization of wilderness areas draws him into the midst of a natural population which allows the existence of vast numbers of biting flies and acarines. Agriculture in dry regions is subject to periodic outbreaks of locusts and grasshoppers which occurred before man's arrival on the scene. In order to feed and shelter himself, man creates an artificial environment which he must maintain. This artificial environment of clearing, field, orchard, woodlot, or forest plantation has adjusted itself to a biotic equilibrium which has come to be considered a "natural balance." But elements in this "natural balance" from time to time achieve numbers which threaten the purpose for which man created the artificial environment. Outbreaks of range or forest insects occur because the existing balance of natural agents temporarily fails to control them. Or endemic populations of field and orchard may not be sufficiently suppressed by the environment to allow primary foodstuffs to grow unblemished enough to please the housewife.

Hence a weapon is needed over and above the biotic equilibrium and its manipulation. It has been provided by insecticidal chemistry, and it is the role of the economic entomologist to use it intelligently. He must not turn it on himself or his domestic animals, or on those wild animals that provide him with food and recreation. Nor must he slay his own allies in the fight against insect pests; he must consider the insectivorous birds and mammals and the insect predators and parasites.

Thus the weapon must be used as a stiletto rather than a scythe. Ideally it should be employed to punch a particular hole in the food chain, which, if it cannot be filled in by neighboring elements of the biota, at least should be done at such a time of season that it does not seriously disturb the biota. To this end the economic entomologist must develop selective poisons for particular arthropod species; or rather, since this is not biochemically likely, he must apply them in such a way and at such a dosage level that they become selective to hit the target species alone.

The reality is far from the ideal. There are many instances of overdosing or misapplication destroying fish, birds, and bees. But a more serious outcome is the insidious reduction in population of the predacious and parasitic arthropods that results from the use of relatively indestructible poisons like arsenicals and DDT, a reduction that generally passes unnoticed until the sin bears its fruit of further economic loss. This may take two forms. On the one hand, the target species may appear to become more resilient, requiring heavier and more frequent applications to keep its numbers down. On the other hand, another new and unexpected pest species may appear as a result of the treatment. These end-results, which may appear puzzling and discouraging at the time, are referable primarily to the failure of the predator and parasite population. Any reduction in their numbers, even if the pest species too are reduced to the same proportionate extent, puts the pest species at an advantage;[185] since not only is the biotic potential (the ability to recover) of the herbivorous pest greater than that of the carnivorous predator or parasite, but also the predator or parasite has less topographical chance of contacting the pest when the numbers are low.

Three techniques have already been tested for killing the pest without killing the parasitic and predacious insects. The first is the application of a non-persistent insecticide at a time when the parasites are protected inside the host species and the predators can largely escape; the nicotine fumigation of field crops for aphid control is an example.[158] The second involves the use of a persistent insecticide whose crystals are coated with a material which eliminates its contact effect for the non-herbivorous beneficial insects, while leaving its stomach toxicity for the herbivorous pest; the addition of degraded cellulose to DDT is an example.[159] The third method is devised to render plants insect-proof with poisons taken up into their internal structure (systemic insecticides), which affect only the phytophagous species. By these means the parasites and predators survive the chemical treatment, so that the biological control elements can become additive to chemical control, instead of being replaced by it.

It may be found that insect pests surviving the chemical control are so quickly and thoroughly controlled by the unaffected beneficial insects that the latter in turn disappear from the area. For example, when the cabbage aphid *Brevicoryne* is completely controlled by nicotine and parasites, there is no honey-dew secretion to support the *Aphidius* which emerge some 3 weeks later, and thus these parasites perish. The syrphid adults, finding no live aphids on which to oviposit, leave the area. Thus migrant *Brevicoryne* which subsequently enter the area encounter no biological check and may produce a severe infestation within 50 days of the total eradication.[158] In less extreme cases it often happens that a scarcity of host species may so reduce the parasite population that the host can reach outbreak numbers before the parasite can overtake it.[61] The reduction of an economic species to low density by chemical control at once increases its biotic potential, as a consequence of the simultaneous reduction of its biological control factors, whether due directly to the insecticide or indirectly to its being starved out. Thus chemical control measures must be continued indefinitely to maintain a low density of the pest.[138]

Just as the survivors of a chemical application may find the biological control agencies less numerous than before, so they may find themselves more resistant to chemical control. It is

not that the chemical has made the susceptible insects more resistant, for they are dead. Rather, the chemical has discovered the favoured few that had a certain margin of resistance and selected them to survive and breed. Normally they would then be eliminated by parasites and predators, to whom this kind of resistance means nothing. But if the chemical treatment has removed the biological control species, the more resistant individuals of the pest species can survive to breed. Already nine species of insect pests have developed strains that are resistant to the insecticide that was responsible for their segregation and preferential survival.[167] The extent to which the various economic insects are capable of developing strains resistant to insecticides depends on their degree of heterozygosity in nature, and how far the heterozygous genes can "add up" to produce resistant genotypes. It is ironic that the economic entomologist has thus been able to speed up evolution to man's own disadvantage.

In the following pages the effect of insecticides on animals (especially fish, birds, and bees), on the balance of the arthropod population, and on the development of resistant strains, will be discussed. Since more complete data have been obtained for DDT than for all other insecticides combined, this compound will be covered first under the headings mentioned, followed by a similar treatment for the other insecticides.

I. EFFECT OF DDT ON THE BALANCE OF NATURE

A. Toxicity to wildlife

Mammals. When applied at the rates usual for insect control, DDT has no measurable effect on the population of wild mammals. An 815-acre area on the Savannah river, South Carolina, to which 0.1 lb acre of DDT was applied every week for 17 weeks, showed no significant difference from the normal,[58] in the population of raccoons, cottontail rabbits, and cotton rats. However, where DDT destroys crayfish, raccoons may leave the creeks because of the absence of this staple dietary item.[57] A forested area on the Patuxent river, Maryland, sprayed with 2 lb DDT in 2 gal oil per acre experienced no significant deviation in the normal population of short-tailed shrew and deer

mice. A small area sprayed at 5 lb/acre supported field mice without adverse effect.[31] The spraying of spruce-fir forest in Algonquin Park, Ontario, at 6 lb/acre did no harm to any species of mammals, either directly or through their feeding on poisoned insects or contaminated fruits in the area. Not until the dosage was experimentally raised to 100 lb/acre were symptoms or mortality induced in mice, shrews, bats, or chipmunks.[122] Feeding experiments to elucidate the chronic toxicity of DDT in the food of wild life showed that symptoms of poisoning did not appear in cottontails or meadow mice (*Microtus pennsylvanicus*) until the content in the food reached 2000 ppm (0.2%); total mortality is reached at 4000 ppm. White-footed mice (*Peromyscus leucopus*) were more resistant, symptoms not showing until 10,000 ppm (1%) was reached.[31] The oral LD_{50} of DDT crystals for the cottontail rabbit was found to be 2000 mg/kg.[27] The acute toxicity to the house mouse is sufficient for DDT dust to be used as a control measure, the mice licking themselves and dying within the day.

Birds. The spraying of forest areas with DDT at dosages of 5 lb/acre or more may cause bird losses ranging up to 90% of the population. It is particularly dangerous in the nesting season, when the birds are tied to their territory—precisely the time at which forest insect control is most effectively carried out. Treatment of deciduous woodland at 5 lb/acre near Scranton, Pennsylvania, and Patuxent, Maryland, resulted in a sharp reduction in bird population, from 128 singing males down to only 2 in an entire 40-acre area; and many dead birds (e.g. warblers, vireos, and tanagers) were found.[34,92] Treatment of coniferous forest in Algonquin Park at 3–4 lb/acre had no effect on the number of occupied territories, but a camp area sprayed at 10 lb/acre exhibited a decided reduction in population.[169] When DDT is applied late in the summer it is relatively harmless; e.g. bark-beetle control was carried out in Wyoming in August at 7.5 lb/acre without untoward effects, since the birds at that time ranged widely and the area was comparatively small. The heavy application of DDT to orchards has remarkably little effect on birds, since the blocks concerned seldom cover large continuous areas.[33] No significant difference in the bird population from that of untreated areas was detectable in hardwood forest

sprayed at 2 lb/acre at Patuxent,[34] at 1 lb/acre at Patuxent and Scranton,[92] and at 0.5 lb/acre in Illinois and New Jersey. The weekly application of 0.1 lb/acre for 17 weeks in South Carolina did not affect the numbers of breeding birds.[58] Treatment of coniferous forest at Black Sturgeon Lake in northwestern Ontario at 1 lb/acre elicited no detectable change in the avian population, although some birds were found showing symptoms of "DDT jitters."[105] This level of dosage may cause the temporary departure of insectivorous species such as swallows and flycatchers. The blanketing of 600 sq mi of coniferous forest in Idaho with 1 lb/acre of DDT resulted in a population decline of only 10% as compared with a check area.[87]

Birds have been killed where large doses of DDT have been used to destroy their insect food. When a 200-acre area in North Carolina was treated with 25 lb/acre of DDT to control Japanese beetle, 42 dead or affected robins and catbirds and 14 abandoned nests were found.[34] The death of pheasants and other game birds in orchards in Washington has been attributed to chronic DDT poisoning of their food.[131] When larvae of spruce budworm were taken from an area sprayed at 1 lb/acre and fed to nestlings, one-fifth of the birds were killed and one-quarter showed symptoms if they had no other diet. There was no evidence of poisoning if the DDT-treated larvae constituted less than half of the diet. Sparrows and vireos were more susceptible than flycatchers or waxwings.[64] The direct spraying of nests and nestlings with a dose equivalent to 5 lb/acre of DDT was without appreciable deleterious effect.[132]

The LD_{50} of DDT for the bobwhite quail is 60–70 mg/kg when dissolved in oil, and 250–300 mg/kg when taken as a solid.[31] This wild bird is apparently more susceptible than the domestic hen, which can tolerate 500 mg/kg without symptoms,[175] and the domestic pigeon, which is not killed until the level reaches 1300 mg/kg.[113] The median lethal dose for starlings was 600 mg/kg for DDT in aqueous suspension.[31] Sparrows may also be killed with DDT,[114] which may be effectively used in grain baits to control both these birds and starlings. For chronic oral poisoning, a concentration of 250 ppm of DDT appears to be the critical dietary level at which mallard and pintail ducks begin to develop symptoms and young bobwhite quail show 50% mor-

tality.[31] Domestic fowl withstand 110 ppm in the diet without untoward effects,[11] but a DDT content of 1000 ppm kills chickens within 10 days.[175] The symptoms of DDT poisoning in a bird such as the quail unfold as follows: violence of feeding actions, the onset of tremors and a lack of appetite, continuous tremors with leg paralysis, and finally prostration.[34,64]

The evidence indicates that DDT, as used in orchards and in field crops where 5 lb or more are applied per acre annually, must reduce the bird population. Aerial spraying of forest defoliators, which requires only 1 lb/acre or at most 2 lb acre, has very little effect on the bird population, any harm being attributable to uneven application. The treatment of large areas with 0.25 lb/acre of DDT for mosquito control is quite harmless to birds, unless performed with great inefficiency.

Amphibia and reptiles. Frogs are more sensitive to DDT poisoning than warm-blooded animals, injections of 150 mg/kg killing them within 72 hr.[57] When sprayed on a forest area in northern Ontario, DDT at 6 lb/acre caused 50% mortality of toads, bullfrogs, and green and mink frogs, and the poisoning of their insectan food supply was sufficient to cause 45% mortality.[120] When ponds were sprayed at 5 lb acre, all frogs and their tadpoles were killed within 5 days; whereas a dosage of 3 lb/acre of DDT did not kill any frogs.[178] Similarly a rate of 2 lb/acre was harmless to frogs, toads, or their tadpoles, but in very shallow ponds these amphibia may succumb to rates of 1 lb/acre. The minimum toxic concentrations for tadpoles of DDT in the field may be taken to be 1 ppm in open water and 0.25 ppm in restricted waters, as against 0.1 ppm in laboratory exposures. On this basis an application of 0.1 lb acre, which gives a concentration of 0.3 ppm in the top 3 in. of water, is safe for amphibia provided the pools exceed this depth.[111] The treatment of ponds at concentrations of 2 ppm or more of DDT has killed water snakes, turtles, and salamanders.[56,66] Garter snakes exposed to a DDT spray of 6 lb acre showed 50% mortality, and one individual died from eating a frog that had fed on insects poisoned by the DDT.[120] Water snakes are killed in small numbers by forest spraying at the 1-lb/acre level.[87]

Fish. DDT is very toxic to fish, the median lethal water concentration for the goldfish (*Carassius auratus*) being 0.06

ppm and the LC_{100} being 0.25 ppm.[67] Northern stream fish appeared to be much more susceptible, the LC_{50} for speckled trout (*Salvelinus fontinalis*) and creek chub (*Serratilus atromaculatus*) being between 0.01 and 0.005 ppm, for the sucker (*Catostomus commersonii*) less than 0.005 ppm, and for young fry of speckled trout less than 0.001 ppm.[112] The minnow (*Gambusia affinis*) is killed by continuous exposure to 0.1 ppm in an aquarium, but in the field 0.25 ppm is required for partial mortality and 1 ppm for complete kill.[111] In a pond treated at 2 ppm of DDT all the top minnows (*Gambusia*) and large-mouthed black bass (*Huro salmoides*) were killed.[56] The young of the Kafue bream (*Tilapia kafuensis*) of Rhodesia were all killed by continuous exposure to 0.014 ppm in aquaria, and in shallow pools (2 ft deep) as much as 70% are killed at concentrations of 0.04 ppm DDT.[151] Species of carp (*Carassius*) in Australia were killed in large numbers in a reservoir containing 0.04 ppm of DDT.[187] It would appear that the extreme sensitivity of fish to low dosages of DDT maintained indefinitely in a restricted water body is a contact effect, possibly on the gills; for the LD_{50} by the oral route for the goldfish is as much as 60–100 mg/kg.[57] When the exposure period is limited to 30 min, pickerel (*Stizostedion*), sucker (*Catostomus*), chub (*Platygobio*), ling (*Lota*), and goldeye (*Amphiodon*) are unaffected by concentrations of 25 ppm;[3] when exposure is limited to 15 min, rainbow trout are unaffected by 30 ppm of DDT.[69]

The characteristic symptoms of DDT poisoning in fish are excitation, and then ataxia, spasms, and paralysis. The poisoned goldfish swims off-balance with its tail lowered, and sometimes upside down; this condition is reversible on removal to fresh water.[56] Later the fish lies on its side, showing convulsions which decrease in intensity until death.[57] DDT-poisoned trout and chub become excited and rise to the surface to gulp air, where they usually contact the oil slick of DDT; they hold this vertical position until their equilibrium is lost and ataxia sets in, followed by tremors and death from failure of respiratory movements.[112]

Area dosages of 6 lb/acre are sufficient to kill the creek chub of the shallow pools at the margins of streams in the northern Ontario forest. In some cases, mortality of speckled trout appears at 4 lb/acre, because of their feeding on the numerous

insects falling from the overhanging trees.[112] In ponds dusted at 5 lb/acre [56] or sprayed at 3 lb/acre,[178] the top minnow *Gambusia* has escaped destruction; minnows of this genus survived mosquito-control operations in Italy in 1944. In tidal areas sprayed at 3 lb/acre, there was no kill of rock (*Roccus*) or menhaden (*Brevoortia*).[178] Of the fish inhabiting the Patuxent river, which bisected an area sprayed at 2 lb/acre, the fallfish (*Leucosomus*), largemouth bass, common shiner (*Notropis*), bluegill sunfish (*Lepomis*), eastern madtom (*Schilbeodes*), and silverling minnow (*Hybognathus*) were killed, whereas the johnny darter (*Boleosoma*) and rosy-sided dace (*Chrosomus*) remained unaffected.[34] When exposed in live boxes under this spray, 80–97% of the bluegills were killed but less than 10% of the yellow perch succumbed.[174]

The aerial application of 1 lb/acre of DDT, the favoured dosage for forest insect control, is definitely hazardous to fish; but the game fish are less susceptible than the inhabitants of stagnant and exposed pools, and the hazard is less the denser the forest cover. In a hardwood forest near Scranton, Pennsylvania, sprayed at 1 lb/acre, a creek was observed onto which about 0.25 lb/acre of DDT had filtered through the leaf canopy; the common shiners, golden shiners, and suckers therein were either killed or affected, but only 1.3% of the brook trout were killed.[34] A much smaller loss of fish is obtained if DDT suspensions are sprayed rather than oil solutions.[88] The dense high coniferous forests of Idaho, sprayed at 1 lb/acre, suffered no losses to the rainbow and cutthroat trouts (*Salmo*) and eastern brook trout (*Salvelinus*) of its streams and lakes; [59] however, cottoids, mountain suckers, and black catfish suffered heavy losses in limited areas.[87] When 1 lb/acre is applied to small ponds, a mortality of up to 60% bluegill sunfish is obtained, although few largemouth black bass and no brook trout succumb. The possibility that it was the bluegill's food that poisoned them was tested by feeding houseflies which had been sprayed at 1 lb/acre, with negative results.[34,171] Goldfish were unaffected by daily feeding upon 25 *Aedes* larvae that had been killed by exposure to 1 ppm of DDT.[68] An aerial application of 0.5 lb/acre in Illinois killed some shiners, dace, and toothed herring. Another application of the same nominal intensity at Island Beach, New

Jersey, succeeded in killing about 100,000 menhaden, killifish, and mullet in the tidal areas; since this was due to the pilot overdosing to allow for a high wind, the dosage figure is meaningless.[170]

TABLE 1. Toxicity of DDT and Analogues to Mosquito Larvae (*Aedes aegypti*) and Goldfish (*Carassius auratus*) [67]

	Aedes		*Carassius*	
Compound	LD_{50}, ppm	LD_{100}, ppm	LD_{50}, ppm	LD_{100}, ppm
p,p′-DDT	0.01	0.05	0.06	0.25
o,p′-DDT	0.40	5.00	1.00	4.00
DDD	0.01	0.05	0.90	2.00
Methoxychlor	0.07	0.20	0.06	0.25

On the assumption that all the spray emitted falls evenly on the water bodies, application of 0.2 lb/acre would give a concentration of 0.04 ppm in pools of 2-ft depth, sufficient to kill young fry.[151] A dosage of 0.1 lb/acre would be safe for fish provided the water exceeded 3 in. in depth.[111] Treatment of reservoirs in the Tennessee Valley at an emission rate of 0.1 lb/acre and a deposit of 0.012 lb/acre had no effect on the fish population, which consisted of bluegills (*Lepomis*), white bass (*Lepibema*), shad (*Dorosoma*), carp (*Cyprinus*), and many other species; their arthropod food supply was not sufficiently impaired to cause a reduction in size or numbers of the fish.[85] Treatment of northern forests with 1 lb/acre of DDT against defoliating insects can be practised without undue hazard to the trout fishing, provided the dosage is applied evenly. Where fish are to be protected, the following considerations may be borne in mind. For a given application of DDT, dusts are least toxic and emulsions are more toxic than solutions.[66] The toxicity is enhanced by high water temperatures, and young fish are more susceptible than old. The effect of DDT on fish may be alleviated by supplementary feeding and by the presence of suspended matter in the water.[7] Anti-mosquito spraying at 0.25–0.5 lb/acre need jeopardize only fish in very shallow pools, such as the courtyard goldfish pools formerly fancied by Chinese bourgeois. Nevertheless, the possible substitution of DDD is worthy of attention, since it is as toxic to the mosquito as DDT but is less toxic to goldfish (Table 1).

However, it is almost as lethal as DDT to the Alaskan grayling, while methoxychlor is half as toxic.[182] Eradication of blackflies may be obtained by treatment with 1 ppm of DDT for 15–30 min. without killing stream or river fish.[3, 86]

Other invertebrates. Species belonging to the phyla Protozoa, Nemathelminthes, Platyhelminthes, Rotifera, Echinodermata, Mollusca, and Annelida are resistant to contact poisoning by DDT, since they lack a chitinous cuticle. Area spraying with DDT at 1–5 lb/acre had no effect on molluscs, oligochaetes, and *Planaria;*[88] however, an aquatic snail (*Physa*), though surviving 0.1 ppm, was killed by a concentration of 1 ppm in ponds.[56] Earthworms (*Lumbricus*) in leaf litter under elms sprayed with DDT ceased their normal activity during fall and spring, but by May they were just as active as in an unsprayed area. The earthworm *Pheretima* was not noticeably reduced in numbers by application of 100 lb/acre to the soil.[61a] Species that are susceptible belong to the Arthropoda, Bryozoa, and those coelenterate genera like *Obelia* that have a chitinous perisarc; *Hydra* is resistant.

Of the arthropods, certain Amphipoda survived exposure to 0.5 ppm for 30 min, but were paralysed by 0.05 ppm maintained for 2 hr.[3] Others succumbed to 0.1 ppm of DDT passing down clear creeks in 30 min. Amphipoda were the only crustacea to show any mortality from aerosol treatment of reservoirs at 0.1 lb/acre.[85] The water flea *Daphnia magna* survived water contaminations below 1 ppm of DDT, at which concentration one-half of the population was paralysed within 32 hr.[1] Anostraca, Cladocera, Conchostraca, and Copepoda were numbered among the victims in streams treated at 0.1 ppm;[86] although with aerial sprays copepods and cladocerans were not particularly susceptible.[162] The plankton species *Daphnia* and *Cyclops* inhabiting ponds located in sprayed areas are less affected than the aquatic insects, and soon increase their numbers.[56, 89] Sprays of 1 lb/acre caused fish to change their diet to include more Crustacea.[89] Certain members of the Entomostraca are unaffected by area sprays of DDT; some species of Hydracarida may survive,[55, 56] but others may succumb.[56] Among the most susceptible arthropods are crayfish (*Astacus* spp.), which suffered heavily from treatments of 1 lb/acre in Idaho[89] and 0.5 lb/acre in Illinois.[34] These

heavily chitinized animals are all killed at 1 ppm, and some die at a level of 0.25 ppm of DDT in the water.[111] Species of Australian crayfish were killed in large numbers in a reservoir containing 0.04 ppm of DDT.[187] Crayfish are poisoned not only by contact but also by eating DDT-poisoned food.[162] Barnacles (Cirripedia), those arthropods which infest wooden timbers of boats and docks, are highly susceptible to poisoning by DDT.[163]

Among the Acarina, ticks are comparatively susceptible, but mites are comparatively resistant to DDT, with the exception of some predacious forms; the effect of this situation on the orchard biota is discussed below. Arachnida are comparatively resistant. When forest is sprayed at 1 lb/acre, only the phalangiids succumb; at 5 lb/acre all exposed spiders are affected or killed.[56, 88] When her web is liberally sprayed with DDT, the black widow (*Latrodectus mactans*) shows jitters in 1 day and dies after 2 days.[184] DDT is the most effective residual poison for *Latrodectus*, followed by chlordane and lindane.[63a] The scorpion *Centrurus* is readily eliminated by residual deposits of DDT.[177] Centipedes (Chilopoda) and sowbugs (Isopoda) are readily killed by DDT aerosols in greenhouses, but spiders are not.

Beneficial or desirable insects. Aquatic insects suffer heavily from DDT applications. Fortunately the larvae of Culicidae and Simuliidae are the most susceptible of all. Anopheline larvae proved to be even more sensitive than culicines at an area dosage of 0.1 lb/acre. Ephemeroptera and Trichoptera are among the groups most sensitive to DDT, followed by Plecoptera and the Chironomidae.[56, 88, 89] Streams flowing through a forest area in Pennsylvania treated at 1 lb/acre (where stream deposits ranged from 0.25 lb/acre in the shaded spots to 0.8 lb/acre in the open stretches) showed 70% overall insect loss when DDT suspensions were used, and 90% when oil solutions were sprayed. In the latter case, Plecoptera and aquatic Hemiptera and beetles joined the casualty list of May flies and caddis flies.[88] The larger nymphs of Odonata and Plecoptera, the Megaloptera, and bottom-feeding Trichoptera were able to survive. The elimination of insect larvae in streams by 1-lb/acre applications in Idaho was found to cause a 50% reduction in fish food,[49] but the species that suffered heavily were found to increase greatly in the fol-

lowing year. In areas treated the preceding year at 4–6 lb/acre, the creek population had returned in 12 months to 40–80% of its normal level, although in one stretch of rapids it remained at only 5% of normal.[162] Treatment of rivers with 0.1 ppm of DDT resulted in an 85% reduction of May flies and stone flies, but the effect disappeared about 20 mi downstream.[3] The larvae of the caddis flies *Hydropsyche* and *Halesus* were unaffected by the passage of 10 ppm of DDT for 15 min.[69] Mosquito-larviciding operations in Canada with DDT at 0.25 lb/acre fail to reduce the population of Odonata, Chaoborini, and the harmless pitcher-plant mosquito *Wyeomyia* to any extent; however, the larvae and adults of Dytiscidae are almost as susceptible as the *Aedes* larvae.[183] Operations in West Africa against *Anopheles* larvae had little effect upon their predators.[26] Aerosol applications in Tennessee at 0.1 lb/acre had no effect on aquatic forms other than Culicidae, but eliminated surface Hemiptera, i.e. *Gerris*, *Trepobates*, and *Hydrometra*.[85]

When a hardwood forest is sprayed with 1 lb/acre of DDT from the air in early summer, the principal victims are small caterpillars, moths, and flies, and psyllids. This, however, does not prevent the normal rise in insect population from making itself felt within a week. When the dosage was increased to 2 lb/acre, the tree caterpillars were eliminated, the calyptrate flies were reduced by 85% and adult moths by 70%, and the leaf-feeding beetles and Hymenoptera were decimated to an undetermined degree. The ground-inhabiting beetles Carabidae, Staphylinidae, and Silphidae were unaffected. The aphids frequenting leaf undersurfaces survived, as did many of their parasites and predators. The population of moths returned to a normal level in 3 weeks, and the Hymenoptera in 4, whereas the higher Diptera did not recover until 8 weeks after the application.[88]

When a second-growth hardwood bush was sprayed at 5 lb/acre of DDT, the parasitic Hymenoptera and Diptera were eliminated along with the forest defoliators. A great reduction was observed in the cicadellids, membracids, and chrysomelids. The ant population was also affected. The insects that escaped were inhabitants of the ground, leaf undersurfaces, or bark crevices (e.g. Collembola); scale insects also survived. The ants recovered their numbers in 1 week, the Hymenoptera took 3 months to

recover 25% of their normal level, and the fly population did not return that year. When a stand of lodgepole pine was sprayed at 7.5 lb/acre of DDT, the entire insect population was reduced by 90%.[88]

B. Toxicity to bees

DDT is highly toxic to the honeybee,[55] the median lethal dose taken orally being approximately 5 micrograms per individual[50] (cf. Table 4). A lethal dose may also be taken up by contact, whereby it is quite toxic,[25] or by residual contact.[60] Concentrations of 0.01% DDT in nectar (queen-cage candy) will kill an entire colony in 2 days. However, as much as 1% DDT in pollen paste has virtually no effect on the colony. A liberal dusting of hive and bees with 20% dust resulted in about 80 casualties, including the queen, but the colony returned to normal in 2 days.[50] Nevertheless two treatments a week apart with both dust and spray are sufficient to eradicate undesirable colonies.[110]

In the field, however, DDT has presented comparatively little hazard to honeybees and is much less dangerous than the arsenical treatments it replaces.[52] It has been shown that bees are much more susceptible to DDT at high temperatures than at low; hence the toxicity in the field is generally less than at the high temperatures in the laboratory or the hive.[79] When 3% or 5% dusts are applied to alfalfa fields in bloom, a proportion of the bees in it (about 25%) are killed directly, but many of them leave the field immediately; the bee population of the field returns to normal in 3–4 days.[119] The "repellent" effect of DDT dusts results in a temporary reduction in bee activity and productivity, but it is more than offset by the increased nectar flow later due to the control of plant bugs on the alfalfa.[168] Brood damage is inconsiderable, the maximum ever observed being 3 frames per colony.[51] Appreciable injury to the field force of bee colonies has been found only when DDT has been used on alfalfa in full bloom. Under these conditions a 28% mortality was reported from Utah when a 3% dust was applied,[180] and dusts containing 10% DDT were much more injurious than this.[53] The apparent repellent effect of DDT is interesting, but is probably referable either to the solvent, or to the disturbance involved in the application, or to an increased activity due to mild

poisoning; it is not comparable to true vapour repellency, because DDT is non-volatile. It must also be stated that, in the period 1945–48, when DDT came into use on field legumes, the wild bee population in many districts of the United States was dropping.

Application of DDT to mustard blossom, and to blooms of apple and cotoneaster, proved apparently harmless to visiting *Apis* and *Bombus*.[189] Heavy applications of DDT to apple blossom in an orchard worked by bees resulted in no higher death rate of adult bees or brood than in an untreated orchard. The replacement of calcium arsenate dust by 5% DDT dust for potato insect control left all bee colonies in a healthy condition, in contrast to the damage wrought by the arsenical.[55] The wild bee *Nomia melanderi* was affected by treatment of alfalfa fields with 3% DDT dust at 20 lb/acre. Although the treated area was repellent, so that only half of the bee population visited the field, in addition the number of active nests was reduced by 15%, and 2% of the estimated population of bees were found dead on the ground.[16]

The spraying of large areas with DDT at 0.2 lb/acre to control mosquitoes had no effect on the bee population in California.[33] Forest spraying from the air with as much as 5 lb/acre in Pennsylvania did not harm beehives in the area.[34] However, the scarcity of bees in Singapore in 1946 has been attributed to the aerial spraying of the city as a malaria and cholera control measure.[146]

Although DDT presents comparatively little danger to bees, certain precautions should be taken, particularly if the more hazardous dusts are used. If possible, applications should be made before blossoms open or after they fall. It is safest to limit operations to the evening, early morning, or dull or rainy days when the bees are not working. Wettable powders should be substituted for dusts where it is feasible to do so.

C. Effect on balance of arthropod populations

The application of DDT to tree and orchard crops has led to an increase in a number of pests where parasites and predators are preferentially reduced by this insecticide. Such pests fall into four groups: (i) Aphids, (ii) tortricid larvae, (iii) coccids, and (iv) Acarina.

Aphids. The treatment of a second-growth hardwood stand with 5 lb acre of DDT in early summer resulted in a general infestation of at least 14 species of aphids. These insects had survived the spray on the undersurfaces of leaves. Their predators (cantharids, mirids, lygaeids, nabids, anthocorids, syrphids, coccinellids, and chrysopids), which had been decimated by exposure to the spray, could not re-establish themselves fast enough to check the outbreak.[88] The substitution of DDT for nicotine sulphate in vineyards in the eastern United States has resulted in an upsurge of *Aphis illinoiensis* and *Phylloxera vitifoliae*.[172] The use of DDT or calcium arsenate on cotton induces infestations of *Aphis gossypii* consequent on the destruction of its coccinellid predators.[10] Application of DDT to sugar cane encourages outbreak of the yellow aphid *Sipha flava*, associated with the destruction of its predators.[100] The destruction of the chalcidoid parasite *Aphelinus mali* by DDT sprays in apple orchards has resulted in infestations of the woolly apple aphis, *Eriosoma lanigerum*, in Washington,[137] British Columbia,[160] and New Zealand. DDT is highly toxic to *Aphidius brassicae*, the parasite of the cabbage aphis; it is harmless to syrphid larvae, but the adults may be killed by the residues or inhibited from ovipositing.[188]

Tortricid larvae. The great rise in population of the red-banded leaf roller, *Argyrotaenia velutinana*, in 1946–49 in the apple orchards of eastern North America is considered to be due to the substitution of DDT for lead arsenate in the spray programme. This new insecticide, while no more effective against the leaf roller than lead arsenate, is considerably more effective against its parasites and predators.[73] In Canada, the increase of *Argyrotaenia* has also been paralleled by a rise of apple maggot (*Rhagoletis pomonella*) sufficient to damage the crop.[160] An increase of *Argyrotaenia* has also been noticed in vineyards since the change from arsenicals to DDT.[172] In Australia the substitution of a DDT schedule for lead arsenate in apple orchards has led to infestations of *Tortrix postvittana*.[111] Another tortricid which leads a protected larval life and is comparatively difficult to kill by a contact insecticide is the spruce budworm (*Choristoneura fumiferana*). In many forest areas it has been observed that where only partial control was obtained with DDT

at 1 lb/acre, the infestation in succeeding years was greater than in areas which had not been sprayed, presumably because of the reduction of parasite control by the DDT. The oriental fruit moth (*Grapholitha molesta*) has shown a marked decrease of parasitism by the braconid *Macrocentrus ancylivorus* since the introduction of DDT into the peach orchards of New York[192] and Ohio.[157] Exposure to DDT residues for 12 hr is sufficient to kill all these parasites, which take up to 36 hr to die.[166] The parasitism of *Grapholitha* larvae in Ohio dropped from the normal 58% down to 37% in 1946 and 23% in 1947. The abrupt drop in parasitism on application of DDT to second-brood larvae on July 24 is shown in Fig. 1. There is evidence that low deposits of DDT, as given by dusts rather than sprays, have little effect on *Grapholitha* but are still lethal to *Macrocentrus*.[157] Deposits from 0.01% suspensions of DDT on peach foliage are toxic to the ichneumonid *Cremastus* and the tachinids *Nemorilla* and *Archytas*. The parasites of another tortricid, the strawberry leaf roller (*Ancylis comptana*), are highly susceptible to DDT.[147]

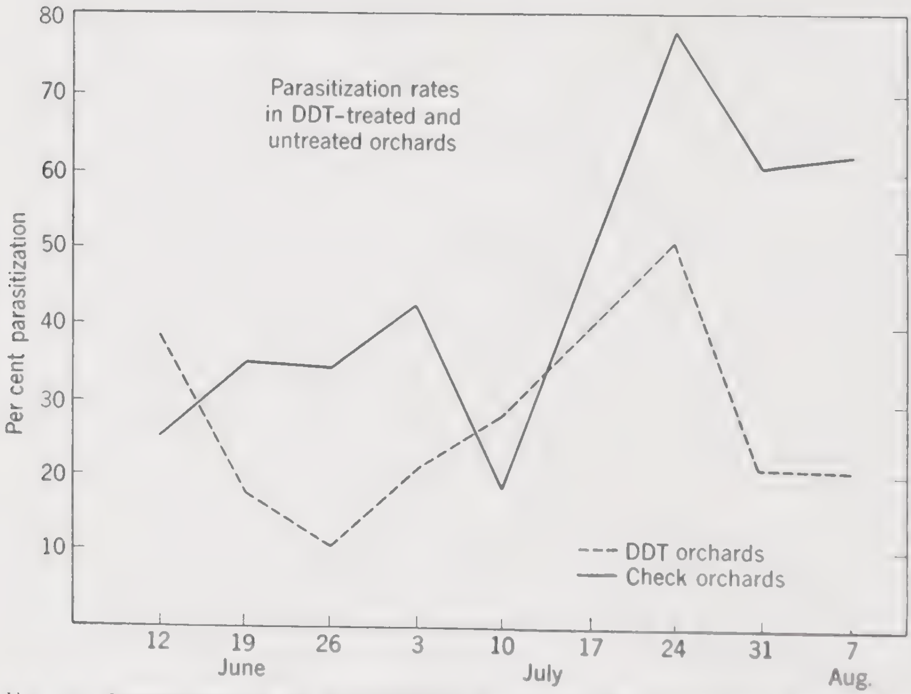

FIG. 1. Parasitization of *Grapholitha* larvae by *Macrocentrus* during the summer spray period. (From Rings and Weaver)

Coccids. The use of DDT sprays in citrus orchards has favoured an increase of the Florida red scale (*Chrysomphalus aonidum*), due not only to its destruction of parasites and predators but also to the residues of the wettable powders providing suitable points of attachment for the scale on the leaves.[145] One year of DDT treatment is enough to cause outbreaks of this red scale to appear in the succeeding two years, accompanied by a rise in the population of *Pseudococcus citri*.[76] In California, DDT has favoured the increase of yellow scale (*Aonidiella citrina*) by killing its encyrtid parasite, *Comperiella fasciata*. Moreover, like the arsenicals, DDT has caused outbreaks of the cottony-cushion scale (*Icerya purchasi*) by killing its coccinellid predator, *Rodolia cardinalis*. On the other hand, applications of DDT dust have had no particularly detrimental effect on *Metaphycus luteolus*, a parasite of the citricola scale.[199] In vineyards, the substitution of DDT for other insecticides has caused the brown scale (*Eulecanium corni*) and the grape mealy bug (*Pseudococcus maritimus*) to come into prominence.[172] In apple orchards, DDT schedules sharply reduce the parasitism of the apple mealy bug (*P. comstocki*), since it is very toxic to *Pseudaphycus*; thus when DDT applications are discontinued the scale, no longer kept within bounds by either the DDT or the parasite, multiplies rapidly.[98] Only if DDT is applied continuously does it fail to increase.[29] The substitution of 0.1% DDT sprays for calcium arsenate in walnut orchards resulted in an upsurge of the frosted scale (*Lecanium pruinosum*) population from 0.5 per twig to 65 per twig.[130] The use of DDT in pear orchards in California induced an increase in the Baker mealy bug (*Pseudococcus* sp.), since it was highly toxic to the lady beetle *Scymnus binaevatus*; its effect on another predator, *Chrysopa californica*, is evidenced by the following comparative population figures: on unsprayed trees 19 *Pseudococcus*, 134 *Chrysopa*; on sprayed trees 713 *Pseudococcus*, 20 *Chrysopa*.[41] In Pennsylvania the DDT treatment of orchards resulted in outbreaks of the European fruit lecanium (*L. corni*); before this insecticide was used, the scales had always been so heavily parasitized that infestations did not develop.[4] In Manila, Philippine Islands, outbreaks of 10 species of coccids followed the repeated antimalarial spraying of the city; the investigators found that they

could be controlled by even heavier applications (2.5% emulsions) of DDT, only to discover that the infestation reappeared 2–4 weeks later.[134]

Acarina. DDT at the dosage levels required for insect control fails to obtain a high mortality of mites. Thus a consequence of spraying broad-leaved woods at 5 lb/acre was the development of an infestation of the spruce spider mite (*Paratetranychus ununguis*) on red maple in the spring of the following year; its release from natural control appeared to have been due to the destruction of its neuropteran predator, *Coniopteryx vicina*, by the DDT.[88]

It is now rather widely accepted that the increase in population of the European red mite (*Paratetranychus pilosus*) and the two-spotted mite (*Tetranychus bimaculatus*) in the apple orchards of eastern North America is due to the destruction of mite predators by DDT.[197] The application of the standard 0.25% suspension of DDT in an Indiana experiment eliminated the coccinellid predator, *Stethorus punctum*, a thing which neither lead arsenate nor nicotine did, and in consequence *Paratetranychus* and *Tetranychus* became very abundant in the DDT plots.[171] This spray was found to give only 50% reduction in population of *Tetranychus bimaculatus* when it was reared free of predators.[197] Infestations of *P. pilosus* have followed the DDT schedule in Maryland,[71] and of *P. pilosus* and *T. schoenei* in Virginia.[97] Investigation showed that the DDT killed *Stethorus punctum*, and that it may prevent the appearance of the predacious mite *Iphidulus* and the predators *Leptothrips* and *Scolothrips* which normally combat the usual increase of the orchard mite population late in the summer. Lead arsenate never prevented their appearance, and sometimes even DDT may not prevent it and consequently there is no mite infestation.[29] A rise in mite population does not always follow DDT application; an experiment in eastern New York obtained no significant difference in population on sprayed as against unsprayed orchards, although in one DDT-sprayed orchard an infestation of red spider mite (*Tetranychus telarius*) appeared in September.[29] Infestations of the clover mite (*Bryobia praetiosa*) follow the applicaton of DDT to apple orchards in the warmer districts of South Australia[102] and the central United States.[129]

The rise of *Paratetranychus* in Ontario is attributed to the destruction of *Stethorus*, *Haplothrips*, and predacious mites of the genus *Typhlodromus*.[160] The similar rise of *Tetranychus pacificus* in Washington and British Columbia has been experimentally duplicated by the use of DDT[136] and is considered to be due to the destruction of predators, particularly *Stethorus picipes*. In Nova Scotia, DDT has proved to be very destructive to *Iphidulus tiliae*, a mite predator of *Paratetranychus*, and to the mirid predators *Diaphnidia* and *Hyaliodes*.[121a]

TABLE 2. EFFECT OF DDT AND TALC ON PARASITES AND PREDATORS OF THE CITRUS RED MITE (*Paratetranychus citri*)[40]

Population per 100 leaves 2 months after application

Spray Suspension	Predators	Mites
12.5% DDT in talc	9.7	2302
Talc alone	32.8	1896
Untreated	28.8	377

An increase of citrus red mite (*Paratetranychus citri*) has been demonstrated in California citrus orchards when they are treated with a suspension of DDT and talc.[40] It is closely associated with the destruction of the predators *Stethorus picipes*, *Oligota oviformis* (Staphyl.), and *Conwentzia hageni* (Neuropt.). A similar increase in the red mite without the decrease in predators is produced by the application of talc alone to foliage (Table 2). It was observed, in the years before the appearance of DDT, that inert dust residues increase the population of citrus red mite, possibly owing to their providing better adherence for mites on the leaves.[91] In Florida citrus orchards, DDT treatment for a single season encouraged infestations of *P. citri* and *Phyllocoptruta oleivorus* in the following two years.[76] In the vineyards of the United States the substitution of DDT for lead arsenate and nicotine has resulted in *Paratetranychus pilosus* and *Tetranychus* spp. becoming a serious problem.[172] There has been a similar rise in peach orchards; in Washington State this has been associated with the destruction of *Hippodamia convergens* and *Coccinella transversoguttata*.[200] The number of egg masses of these predators after DDT sprays, as compared with cryolite or lead arsenate sprays, is as follows:

Spray	Dormant	Calyx
DDT, 0.1%	6	0
Cryolite, 0.3%	320	173
Basic lead arsenate, 0.3%	341	211

The use of DDT sprays in walnut orchards has led to an increase of *T. bimaculatus* and *P. pilosus* in California.[129] The dusting of cotton with DDT has led to outbreaks of *Tetranychus* mites.[16,129] In New South Wales, the use of DDT on beans has encouraged outbreaks of *T. telarius*, and on tomatoes has induced severe infestations of *Phyllocoptrutes lycopersici*.[84] A horrible example is furnished by an attempt to control mosquitoes with a 0.1% DDT suspension in a wooded glade in Connecticut; it failed to control the adult mosquito population, but it led to an outbreak of the oak red mite (*P. bicolor*) on the maple and oak trees sufficient to turn the foliage yellow, and to an infestation of *T. telarius* on a hydrangea hedge sufficiently heavy to defoliate it.[24]

D. Appearance of resistant strains of susceptible species

The housefly (*Musca domestica*). By 1946, 2 years after the introduction of DDT into Italy, houseflies resistant to control were noted near Rome and Naples, and in other parts of the country.[13,131] A varietal name, *M. domestica tiberina*, was suggested for this strain.[161] Also in 1946 a highly resistant strain was observed at Arnas in northern Sweden, where DDT had not been used before.[191] In 1947, resistance appeared in Cairo, Egypt, and Ellenville, New York.[7] In 1948 DDT-resistant houseflies were prevalent in certain districts of California.[123] The failure of DDT to control houseflies in 1947–48 in Texas, Georgia, North Carolina, and Florida resulted in the discovery of several strains that were more resistant than the normal.[194] Examination of flies in 1948 from six barns in New Jersey that had been sprayed early that summer showed that three of the stocks were only half to two-thirds controlled by doses that killed all normal houseflies.[81] Flies collected in the field in Florida were all more resistant than the laboratory strain, and both DDT and methoxychlor were proving ineffective as barn sprays.[194] Field-collected flies in Ontario and Quebec in 1949–1950 were all more resistant than the laboratory strain, the most resistant

strain being found at Granby, Quebec. It is the experience in barn-spray programmes that the late-season flies are more resistant than the spring populations. Examination of flies in 1949 from a ranch in California to which DDT, BHC, and dieldrin had been successively applied 6 months earlier showed that they were resistant to all three insecticides.[123a]

The degree of resistance in the Swedish resistant stock was such that its median lethal dose of DDT was 2.5–5 μg, as against 0.025 μg for normal flies.[194] The New York stock, 10 generations after artificial breeding without exposure to DDT, showed only 15% mortality from DDT residues that kill 100% of the normal line.[8] The Swedish resistant stock was more hardy to extreme temperatures than the normal (in this case a laboratory stock at Basle, Switzerland). They also were more heavily pigmented and showed morphological differences in their tarsi, the joints being larger, the hair-tuft stiffer, and the pulvilli and articular membranes 30% thicker.[194]

Resistant strains of *Musca* have also been developed by artificial selection in the laboratory. Every generation was space-sprayed with the LD_{90} of DDT, and the survivors produced the next generation. After 14 generations of such selection this strain showed only 34% mortality to a dosage that killed 69% of the normal laboratory strain.[118] By the thirty-fifth generation these flies survived a dose double the original LD_{100}, and a proportion survived a triple dose. In another investigation, selection by applying the LD_{50} to each successive generation of adults resulted in a measurable increase of resistance in the F_2 to F_{10} generations.[9] Laboratory strains developed in Illinois by applying the DDT to the larvae as well as the adults did not begin to show increase in resistance until the F_{12}, after which it rapidly increased to the F_{18}, where a constant level was reached.[24a] DDT-resistant strains of *Drosophila melanogaster* and of the fruit-moth parasite *Macrocentrus ancylivorus* have been developed by laboratory selection.*

The Ellenville wild DDT-resistant strain showed a parallel increase in resistance to methoxychlor and DDD. It also appeared to have an enhanced resistance, but to a less degree, to chlordane and parathion. There was no difference from the nor-

* Dominion Parasite Laboratory, Belleville, Canada.

mal in the response to toxaphene.[7] The resistant flies were able to recover repeatedly from knockdown by DDT.[8] The California strains showed a parallel increase in resistance to the DDT analogues, but not materially to other insecticides (Table 3). For

TABLE 3. RESISTANCE OF CALIFORNIA STRAINS OF THE HOUSEFLY TO DDT AND OTHER CONTACT INSECTICIDES IN 1948 [123]

Median lethal dose, μg per fly

Insecticide	Laboratory	Riverside	Ontario	San José	Bellflower
DDT	0.02	0.5	0.5	0.7	10.0
DDD	0.1	....	....	....	20.0
Methoxychlor	0.07	0.3	0.3	0.3	1.0
Toxaphene	0.2	0.5	0.5	0.4	0.6
Lindane	0.01	0.06	0.05	0.05	0.08
Heptachlor	0.03	0.07	0.07	0.07	0.06
Pyrethrins	1	2	2	2	1

example, the resistance of the Bellflower strain as compared to laboratory flies was increased by 500 times to DDT, 200 to DDD, 14 to methoxychlor, 8 to lindane, 3 to toxaphene, 2 to heptachlor, and not at all to pyrethrins. It was found that the increased resistance of the resistant strains over the normal was maintained if the insecticide was applied by injection.[123] The laboratory-selected strains showed the same order of resistance (when compared one with the others) to chlordane, toxaphene, *Thanite*, rotenone, and pyrethrum as they did to DDT.[9, 196] Florida strains of houseflies showed no increase in resistance to BHC or chlordane if they were only 10–20 times as resistant to DDT as normal strains; but those that were highly resistant to DDT were resistant to other insecticides in much the same pattern as the California houseflies described above.[107] The DDT-resistant strains developed in the University of Illinois laboratories were equally resistant to methoxychlor, and showed some degree of resistance to lindane, dieldrin, para-oxon and other insecticides.[214]

In contrast to the field-collected strain at Arnas, a laboratory-selected resistant strain developed at Cornell University exhibited a pulvillar cuticle of normal thickness and there was no abnormality in the histological structure. But there was evidence that those flies with a longer larval and pupal life were the most

resistant to DDT. The Bellflower resistant strain did not differ from the normal in cuticular thickness, nor was there any difference in general vigour.[123c] A careful comparison of the physiology of resistant and susceptible houseflies showed that both strains absorb DDT through the cuticle at the same rate, but that the resistant strain can rapidly metabolize it to DDE (the dichloroethylene analogue) and a little DDA, while the susceptible strain is unable to perform this detoxification.[171a] This immunity can also be conferred by methoxychlor, so that resistance to DDT and to methoxychlor is congruent.* That the resistance factor may be synonymous with the ability to dehydrochlorinate the DDT molecule is also indicated by the fact that DDT-resistant strains are no less susceptible to dichlorodiphenylnitropropane than are the normal strains. The ability of resistant flies to dehydrochlorinate DDT is destroyed by poisoning with piperonylcyclonene.[146a] The Ellenville resistant strain has an appreciably higher content of cytochrome oxidase than the normal.[161a] Strains which have developed a limited amount of tolerance are readily knocked down by DDT but completely recover from it, while the thoroughly resistant strains are not knocked down at all.[24a]

It has been found at Savannah, Georgia, that laboratory-selected resistant strains lost their resistance if subsequently bred in the absence of DDT. A similar result was obtained with field-collected resistant strains at Cornell University.[151a] The resistance of DDT-resistant flies collected in Florida was found to fluctuate as they are bred through a long series of generations.[101a] The resistant strains from Riverside, California, have proved capable of maintaining their resistance unchanged for more than 30 generations,[183a] while the laboratory-selected strains at the University of Illinois have maintained their resistance after 30 generations of freedom from DDT. Since the hybrid resulting from a cross between resistant and susceptible parents shows an intermediate tolerance, the result of the reciprocal cross being identical, it is concluded that the genetic factor is not sex-linked. Since the succeeding generations of the hybrid show a variability in the dosage-mortality response much greater than the parent

*However, houseflies collected in California and Texas in 1950 showed generally normal susceptibility to methoxychlor.

strains, it is concluded that multiple genes are involved in the development of resistance. As far as development of resistance in the field is concerned, the Illinois workers conclude that the larvicidal effect is considerable, and that in some cases the habits of the fly may change to make it less restless or more attracted to the lower parts of buildings.[24a]

The filter fly (*Psychoda alternata*). Larvae of this species in Illinois were discovered in 1949 to be resistant to doses of DDT that had controlled them in the previous two years.[24a]

Mosquitoes (*Culicidae* spp.). Resistant strains have not been as conspicuous in the case of mosquitoes as in the housefly, but nevertheless there is some evidence that they may arise. Larvae of *Culex pipiens* taken in 1947 from the Pontine marshes near Rome, which have frequently been treated with DDT, proved to be more DDT-resistant than a laboratory strain.[5] The existence of resistant strains of *Anopheles* has been acknowledged,[5] although the Mexican species *A. pseudopunctipennis* was not resistant after 3 years of exposure to DDT.[104a] In 1949, larval populations of salt-marsh mosquitoes (*Aedes taeniorhynchus* and *sollicitans*) at Cocoa Beach, Brevard county, Florida, proved to be resistant to DDT treatments which had adequately controlled their predecessors in the preceding 4 years;[41a] in the laboratory they proved to show 18% mortality to concentrations that killed 90% of normal populations.[104a] In the same year, larval populations of *Culex* and *Aedes* had proved resistant to DDT in Kern county, California.

II. EFFECT OF INSECTICIDES (OTHER THAN DDT) ON THE BALANCE OF NATURE

A. Toxicity to wildlife

Pyrethrins. These poisons are toxic to all invertebrates with the exception of Protozoa. They are toxic also to fish, sticklebacks being killed by concentrations of 0.3 ppm in 4 hr.[28] However, in the field they are harmful only on direct contact. Their toxicity to land reptiles and amphibia is slight, and to birds and mammals it is negligible in practice.

Nicotine. This alkaloid is toxic to all invertebrates including Protozoa, the toxicity increasing with the nervous complexity of

the animals.[78] It is toxic to fish; but since 100 ppm is required to kill mosquito larvae,[148] nicotine is not applied to water in practice. It is highly toxic to birds, but its volatile nature in the field leaves little practical hazard, except possibly in the case of its stable salts.

Rotenone. The derris poisons are toxic to aquatic invertebrates and protozoa, producing symptoms of anoxia.[179] Rotenone is highly poisonous to fish, 0.027 ppm killing goldfish in 6 hr; since 5 ppm is required to kill *Culex* larvae,[148] it is not normally used for treatment of breeding areas. There is an extensive literature on the use of rotenone and derris as piscicides. Rotenone is of moderate toxicity to birds, the oral LD_{50} figures for nestlings being as follows: song and chipping sparrows, 120 mg/kg; American robin and English sparrow, 200 mg/kg; pheasants, 850 mg/kg; and chickens, 1000 mg/kg. Older birds are more resistant, the LD_{50} figures being these: English sparrow, 850 mg/kg; pheasants, 1200 mg/kg; and chickens, 3000 mg/kg. Ground derris root is 25 times as toxic as the pure rotenone (0.75%) it contains. It would take 10 cabbage worms heavily dusted with derris to kill robin nestlings, and 65 to kill a young pheasant; the pheasant, however, is not insectivorous but mainly a seed-eater.[37]

Petroleum oils. Kerosene as used for mosquito larviciding has been found to kill Amphipoda alone among aquatic animals.[14] In the 0.5 gal/acre concentrations now used with DDT for mosquito and blackfly control, it is unlikely that the oil in itself has any effect on aquatic organisms.

Arsenicals. Paris green as dusted on water bodies is nearly specific for mosquito larvae, being harmless to most of the other aquatic organisms, although there is some evidence that it disturbs the metabolism of fish.[14] It does not persist in the water and is probably removed by its conversion to arsines and loss by volatilization. Sodium arsenite is non-toxic to fish at 4 ppm. Birds appear to be quite resistant to lead arsenate poisoning, for chickens can tolerate up to 830 mg daily for 2 months[176] and may be kept without harm in orchards sprayed at 25 lb/acre. However, the use of calcium arsenate and Paris green for potato-beetle control in France resulted in the death of many wild birds

and domestic hens feeding on the poisoned insects; pheasant and partridge were not affected, since they did not eat the beetles.[27]

Sodium arsenite is highly toxic to animals. When dusts were applied from aircraft in Africa in the 1930's against locusts, livestock were moved out of the area; nevertheless wild game were killed, including a specimen of the rare white rhinoceros. Sodium arsenite bait was the cause of Franklin's gulls in Manibota dying from eating poisoned grasshoppers. Calcium arsenate has been extensively applied from aircraft to forests in Europe and North America and has proved entirely harmless to birds and wild animals when applied at dosages between 20 and 30 lb/acre.[169] Nevertheless, a case of extensive mortality of forest animals ascribed to this insecticide was described from Haste, Germany, in 1926.[38] A review of 20 years of forest-dusting operations discounts the injurious effects of calcium arsenate on forest life.[181] However, accidents sometimes happen with this material, such as the poisoning of cattle when the aircraft's hopper is emptied before landing.

Chlorinated hydrocarbons. BHC is less toxic than DDT to fish, a concentration of 0.45 ppm being tolerated by bluegills.[11] However, BHC was found to be more toxic than DDT to pike and other northern fish. The gamma isomer is toxic to fish at 0.05 ppm, the delta at 0.2 ppm, and the beta at 2 ppm.[33] Lindane at 1–10 ppm killed rainbow trout, whereas 30 ppm of DDT did not, for 15-min exposures.[69] Trichlorobenzene, a weedicide, is toxic to fish at the dosages required to kill aquatic plants; it may occur as an impurity or breakdown product of BHC. Lindane is lethal to snails, and the delta isomer is exceptionally toxic.[80] BHC is highly toxic to isopods but has little effect on earthworms.[132b] In comparison with DDT (whose LD_{50} is approximately 0.05 ppm, field applications of 1 lb/acre proving toxic to fish), chlordane is variously reported as more toxic,[182] less toxic,[11] or equitoxic.[33] Toxaphene is more toxic to fish than DDT, killing at 0.005–0.01 ppm.[11] Exposures of rainbow trout to 1–10 ppm of toxaphene for 15 min were lethal.[69] Area sprays of toxaphene at 1.5 lb/acre have caused slight mortality of frogs and salamanders.[33] The chlorinated hydrocarbons tested have proved to be less toxic than DDT to birds; when bobwhite quail were fed at the rate of 250 ppm in the diet for 6 weeks (a level

which kills 15–50% with DDT) no birds were killed with BHC or toxaphene, and only 10% with DDD.[186] Grasshopper control with chlordane or toxaphene at 1.5 lb/acre in the western United States yielded no instances of the poisoning of birds or wild mammals.[33]

Organic phosphates. TEPP is comparable in toxicity with DDT to fish.[11] Parathion was found to be approximately 10 times as toxic as DDT to rainbow trout, salmon, and grayling in Alaska,[182] but less toxic than DDT to stickleback and pike in Canada. Application of parathion at 0.25 lb/acre to wheat-fields in Oklahoma did not kill birds or other wildlife. The only cases of mammalian poisoning by application of parathion in the field concern *Homo sapiens* himself.

B. Toxicity to bees

Arsenicals are extremely toxic to the honeybee. The minimum lethal dose has been variously set between 0.2 and 0.5 microgram (as As_2O_3) per bee.[18,126] In pome orchards, where bees perform an essential part in the fertilization and production of fruit, lead arsenate and other arsenicals are not applied until the apple blossoms are about three-quarters over; this is the petal-fall or calyx spray. For safety, the hives should be closed during this application. If the insecticide is applied too early, bees will collect arsenic in both nectar and pollen, and thus create the hazard not only of self-poisoning but also of poisoning the hive. Bees do not discriminate between sprayed and unsprayed trees and will die within 3 hr of gathering lead arsenate from open blossoms. Bees caged with apple trees in bloom showed 69% mortality when the tree had been sprayed with lead arsenate, and 49% when it had been dusted with lead arsenate, as against 19% mortality on an unsprayed tree.[153]

Calcium arsenate is also highly toxic to bees and is not applied to field crops whose flowers are visited by these insects. When calcium arsenate was dusted from aircraft in California onto corn or tomatoes, which are not visited by bees, the drift of dust to adjoining areas, then supporting various flowers visited by bees, was sufficient to kill 3000 colonies in the Imperial Valley between 1931 and 1934[19] and to poison 1500 hives in a single county in 1943.[18] Hives over a mile away from the dusting operations

were seriously injured.[51] Calcium arsenate dusts applied at 20 lb/acre to control forest insects were found to be extremely hazardous to bees in Germany, 150 colonies being killed in one operation.[152] Heavy losses to bees from arsenicals applied to potatoes were reported from the Yakima Valley, Washington, in 1934.[164]

TABLE 4. ORAL TOXICITY OF ARSENICALS AND FLUORINE COMPOUNDS TO THE HONEYBEE (*Apis mellifica*)

Arsenicals, as As	Median Lethal Dose, μg per bee	Fluorine Compounds, as F	Median Lethal Dose, μg per bee
Sodium arsenate [108]	1.8	Sodium fluoride [17]	6.0
Calcium arsenate [108]	0.7	Sodium fluosilicate [12]	24.0
Acid lead arsenate [12]	5.0	Cryolite [12]	4.2

Cryolite applications also are highly hazardous to bees, like most inorganic poisons which are normally applied in large amounts to control injurious insects. The oral toxicity of fluorine compounds and arsenicals to bees is shown in Table 4. Of these calcium arsenate, a material of variable composition, shows the highest toxicity. The coarse particles (18–28 μ) are much less toxic than the fine particles (2–3 μ in diameter); lead arsenate of 28-μ mean diameter shows an LD_{50} as high as 185 micrograms per individual bee.[12]

The organic insecticides derived from plants—nicotine, pyrethrum, rotenone, and others—normally present little hazard to honeybees. Nicotine is not highly toxic, the oral LD_{50} being 60 micrograms per bee. It has been found to be virtually harmless in the field [12] and has been suspected of acting as a repellent in orchards.[20] Pyrethrum is highly toxic, the oral LD_{50} being 0.3 microgram per bee; [18] when directly sprayed, 0.001% solutions are toxic. However, the extensive use of pyrethrum in cranberry bogs caused only a few cases of bee poisoning.[164] Sprays of pyrethrum with synergist were found to be practically harmless, the bees recovering from any knockdown that occurred.[85] It is considered quite safe to use spray concentrations up to 0.01% in the field, and dust concentrations up to 0.02%, since pyrethrin-contaminated water is not drunk by bees, and the insecticide

is completely destroyed after a day in the open.[18] Rotenone is also very toxic, the oral LD_{50} being 0.6 microgram per bee; when directly sprayed, 0.125% solutions are moderately toxic. The applications of rotenone to raspberry blossoms caused destruction of bees in the field.[164] Derris dust was lethal when applied to lima beans in full bloom.[59a] However, if blossom time is avoided, sprays of up to 0.04% and dusts of up to 1.75% rotenone content may be applied without hazard.[19] The botanical insecticide ryania is only slightly toxic by contact to bees.[25] Sabadilla, however, is highly toxic,[55] dusted alfalfa fields showing a complete kill of bees, but there is no residual effect.[51]

The dinitro compounds DNOC and DNCHP are highly toxic to bees.[55] Their application to citrus orchards has left windrows of dead workers;[51] but in apple orchards little damage to bees or brood has been reported, since these insecticides did not contaminate pollen or nectar to any extent.[70] The organic insecticides xanthone and phenothiazine are virtually non-toxic to bees.[12,55]

Methoxychlor is only slightly toxic to bees orally or by contact, but is quite highly toxic upon residual contact; its hazards are slightly less than that of DDT.[55] DDD is one of the least toxic of the chlorinated hydrocarbons to bees, although the oral m.l.d. is 16 μg per insect, and it can kill by residual contact.[52] Benzene hexachloride is highly toxic orally[55] (see Table 5) and by contact,[25] and can when directly applied kill a colony in a few hours.[52] Applications of BHC on blossom of apple and other plants were extremely poisonous to visiting *Apis* and *Bombus* and remained so for 3 days.[189]

TABLE 5. Oral Toxicity of Chlorinated Hydrocarbons and Organic Phosphates to the Honeybee[53]

Chlorinated Hydrocarbons	Median Lethal Dose, μg per bee	Organic Phosphates	Median Lethal Dose, μg per bee
DDT	4.6	Toxaphene	22.0
DDD	16.0	HETP	0.29
BHC (90% gamma)	0.15	TEPP	0.75
Chlordane	1.2	Parathion	0.07

The evidence as to the toxicity of chlordane to bees is at present conflicting. In one investigation technical chlordane proved

to be a stomach poison, highly toxic by contact and showing considerable fumigant action.[52] In another series of tests, it failed to kill a single bee by stomach, contact, or residual contact.[7] A third investigation showed chlordane to be slightly toxic by contact.[25] Dusts of technical chlordane applied to alfalfa have reduced the field force by 50–80%.[53] Treatment of fields in blossom by 5% chlordane dusts killed 25% of the field bees, about the same result as with DDT.[180] When applied in oil around the hives this insecticide can kill their occupants by fumigant effect.[53] Another chlorinated terpene, aldrin, was highly toxic both orally (with an LD_{50} of 0.25 μg per bee) and by contact, and also showed vapour kill.[53] Toxaphene would appear to be the least poisonous of the chlorinated hydrocarbon insecticides to bees, both by mouth[53] and by contact.[25] The treatment of alfalfa in bloom by 10% dusts resulted in less than 10% mortality.[180]

Hexaethyl tetraphosphate and tetraethyl pyrophosphate have a high order of stomach and contact toxicity to bees.[25,52,53] HETP has no residual effect, while deposits of TEPP may kill for 2 days after their application. Parathion is the most toxic compound yet observed for bees. In addition to a high stomach and contact toxicity,[25] it exerts a considerable fumigant effect.[52] The hazard it presents to bees is equal to that of calcium arsenate.[79] Treatment of blossoming alfalfa fields with 1% parathion dust resulted in 40% mortality of the field force.[180] A bibliography has recently been published covering the effect of insecticides on bees.[135a]

C. Effect on balance of arthropod populations

Hydrogen cyanide. The fumigation of citrus trees with hydrogen cyanide achieves complete control of scale insects in the nymphal stage and a partial kill of their eggs and adults. Concomitantly it only partially eliminates the coccinellid predators;[199] many have been observed to fall to the ground and escape the highest gas concentrations within the tent.[64] Many parasites emerge normally from the scales killed by the hydrogen cyanide. *Cryptochaetum*, a dipterous parasite of *Icerya*, has been observed to do this;[63] and chalcid parasites emerged from a *Lecanium* that had been exposed to saturated hydrogen cyanide

vapour for 18 hr.[77] The parasite, having survived within the tissues of the insect, can emerge into an environment now free of the insecticide.

Tar distillates. The winter application of tar distillates in apple orchards effects a complete kill of the parasite *Aphelinus mali* within the egg of the woolly apple aphid,[30] an observation made both in Germany and in New South Wales.[139] A comparison made in England between untreated orchards and those sprayed with 8% tar-oil wash (plus arsenicals and fungicides) showed that the latter almost completely lacked any Hemiptera, since the tar oil had killed the hibernating adults. Only the apple capsid *Plesiocoris* and various coleopteran species were common to both. Curiously enough, the fruit-tree red spider (*Metatetranychus ulmi*) was present only in the sprayed orchard.[124]

Petroleum oils. Oil sprays in apple orchards have been found in the United States to decrease the population of both *Ascogaster* and *Trichogramma*, parasites of the codling moth.[30] The addition of oil to nicotine cover sprays reduced the second-brood parasitism of codling-moth larvae by *Ascogaster* from 33% down to 25%.[46] The application of petroleum oil to control the pine tortoise scale (*Toumeyella numismaticum*) in Minnesota was accompanied by the disappearance of its coccinellid predators, principally *Hyperaspis binotata*, possibly because of its repellent effect.[143] The use of kerosene sprays in Malaya resulted in an infestation of the citrus blackfly (*Aleurocanthus woglumi*) on the sprayed trees but not on the surrounding untreated trees.[30] The two decades 1920–40 in the California citrus region, which witnessed the extensive application of white oil (Volck) sprays, also saw the disappearance of the coccinellids *Hyperaspis*, *Rodolia*, and *Orcus*, and a diminution in numbers of the chrysopid *Sympherobius*. Also species of red spider (*Tetranychus* spp.) appeared in the interior of the state to cause damage as they had never done before.[199] However, in Nova Scotia apple orchards, summer oils were as detrimental to the phytophagous mites as they were to their predators.[121a] (Table 7).

Lead arsenate. In the 1930's it was observed in the orchards of the eastern United States that the use of arsenicals and of cryolite decreased the parasitism of *Carpocapsa* by its principal

parasite *Ascogaster*.[30] Even spray programmes that failed to control the codling moth nevertheless greatly reduced the numbers of its parasites.[32] From 1930 to 1935 the population of *Ascogaster carpocapsae* in New York orchards that had been sprayed with lead arsenate (and lime-sulphur) was between one-half and one-third of that in unsprayed orchards. However, the difference between sprayed and unsprayed orchards in Ontario was non-existent in 1939–41, although it appeared in 1942.[23] In New Jersey, the larval parasitism by *Ascogaster* in orchards heavily sprayed with lead arsenate was 7–17%, as against 71% in unsprayed orchards.[17] That it was the residue of lead arsenate on the foliage which was responsible for the reduction was experimentally shown, for females of *Ascogaster* confined with residues parasitized two-thirds to one-half as many *Carpocapsa* eggs as the normal,[35] although their longevity was not affected.[23]

TABLE 6. PARASITE AND PREDATOR POPULATION IN ORCHARDS TREATED AND UNTREATED WITH LEAD ARSENATE COVER SPRAY FOR CONTROL OF CODLING MOTH [101]

Average figures for 3 years, 1938–40

	Untreated	Treated
Percentage of eggs parasitized by *Trichogramma minutum*:	13.9	5.7
Percentage of larvae and pupae parasitized by *Ascogaster*:	4.5	1.4
Percentage of eggs eaten by *Leptothrips mali*:	12.1	8.2
Predators in soil, mainly *Harpalus* and *Calathus*:	2060	1687
Ant colonies, mainly *Aphaenogaster* and *Solenopsis*:	1096	624
Percentage of sound fruit (harvest + drop):	34.6	67.0

The egg parasite *Trichogramma minutum* had been considered not to be affected by arsenicals, but only by dormant sprays.[34] However, New Jersey orchards heavily sprayed with lead arsenate showed only 3–5% egg parasitism by *Trichogramma* as against 55–64% in unsprayed orchards.[17] A comparison of two orchards in West Virginia, both of which had received similar dormant and calyx sprays, but one of which lacked the 3–5 cover sprays with lead arsenate (and nicotine) that the other had, showed that this insecticide had the effect of reducing the parasitism of codling-moth eggs by *Trichogramma* (Table 6). The lead arsenate treatment also reduced the population of predacious ants and the percentage of predatism of eggs by *Leptothrips*. The population of predacious ground beetles was slightly

less in the cover-sprayed orchard. The percentage of larval parasitism by *Ascogaster* in the orchard treated with lead arsenate was one-third of that where no arsenical had been applied, but even there the figure was ineffectively low.[101] The application of lead arsenate cover sprays throughout the summer was found to reduce the parasitism of the apple leaf hopper (*Empoasca mali*) by *Aphelopus* from 46% down to 0.3%.[17] In California citrus orchards, arsenicals have favoured the increase of cottony-cushion scale by killing the coccinellid *Rodolia*.[199] It is of interest to note that tartar emetic sprays, when applied against the citrus thrips, do not decrease field populations of the yellow scale's parasite, *Comperiella bifasciata*.[90] In German forests, the dusting of arsenicals decreased the natural parasitism of the nun moth (*Lymantria monacha*).[71] However, lead arsenate sprays do not seriously affect the egg parasite *Aphelinus*.[30] The application of lead arsenate in apple orchards does not adversely affect the predacious mite *Iphidulus*, but is very detrimental to *Anystis;* cryolite is without effect on orchard mites and their predators[121a] (Table 7).

Sulphur. Lime-sulphur sprays applied as a fungicide for apple scab have been found not to affect the egg parasites *Trichogramma*[30] and *Aphelinus*.[139] But the addition of lime-sulphur to lead arsenate in residual sprays on apple foliage halved the percentage of parasitism of codling-moth larvae by *Ascogaster*.[23] There is also evidence that lime-sulphur reduced the population of *Ascogaster* in New York orchards.[32] The substitution of elemental sulphur for lime-sulphur in Nova Scotia in 1932 resulted in an increase in the oystershell scale (*Lepidosaphes ulmi*), because of its lethal effect on *Aphelinus* and on the acarine predator *Hemisarcoptes*, coupled with its inadequacy to kill the scale.[121] Sulphur is also toxic to the predator *Leptothrips mali*. Since elemental sulphur destroys the acarine *Iphidulus* and many other predators of the European red mite (*Metatetranychus*), that species also increases. On the other hand, the clover mite (*Bryobia*) does not increase, because sulphur is more detrimental to it than to its predators[121a] (Table 7). The increase of scale or red mite may be forestalled by the substitution of copper compounds for elemental sulphur in the fungicide spray programme. There is also good evidence that the use of sulphur instead of copper salts for fungicide causes an increase

of codling-moth infestation in Nova Scotia, presumably as a result of its effect on the parasites of *Carpocapsa*.[149] The general effect of sulphur treatment of an orchard is to decrease greatly the number of insect species inhabiting it, leaving certain pests entirely free of their predator stock; the copper fungicides do not eliminate species.[150]

TABLE 7. Effect of Spray Materials on Orchard Populations of Mites [121a] and Their Predators

Det.: material detrimental to the population; Ind.: material comparatively indifferent to the population.

	Elemental Sulphur	Summer Oil	Nicotine Sulphate	Fixed Nicotine	Lead Arsenate	Synthetic Cryolite
Plant-feeding mites						
Metatetranychus ulmi *	Ind.	Det.	Ind.	Ind.	Ind.	Ind.
Bryobia praetiosa	Det.	Det.	Ind.	Ind.	Ind.	Ind.
Predacious mites						
Iphidulus tiliae †	Det.	Det.	Ind.‡	Ind.‡	Ind.	Ind.
Mediolata novae-scotiae	Det.	....	....	....	Ind.	Ind.
Anystis agilis	Det.‡	....	....	....	Det.	Ind.‡
Predacious thrips						
Haplothrips faurei	Det.	Det.‡	Ind.	Ind.	Ind.	Ind.
Leptothrips mali	....	....	Ind.	Ind.	Ind.	Ind.
Zygothrips minutus	Det.	....		....	....	
Predacious mirids						
Diaphnidia pellucida	Ind.	Det.	Det.	Det.	Ind.	Ind.
Hyaliodes faurei	Ind.	....	Det.	Det.	Ind.	Ind.
Campylomma verbasci	Ind.	....	Det.	....	Ind.	Ind.
Pilophorus perplexus	Det.	....	....	....	Ind.	

* = *Paratetranychus pilosus.*
† = *Seiulus pomi.*
‡ Rating still tentative.

Nicotine. When nicotine dust was used for control of aphids on melons it was observed to be harmless to the predacious syrphid larvae and to the coccinellid *Hippodamia convergens* and to reduce only partially the numbers of the parasite *Aphidius*.[144] Similar observations have been repeated in the laboratory.[188] In apple orchards in New South Wales nicotine sulphate did not affect *Aphelinus* at all.[139] In New Jersey, the substitution of nicotine cover sprays for lead arsenate allowed the parasitism of codling moth by *Ascogaster* to rise from 8–10% in the first brood to 33% in the second-brood larvae; with lead arsenate the parasitism rose only to 15%.[16] In English fields of brussels sprouts, the cabbage aphis *Brevicoryne* was 87–99.9% eliminated by nicotine vapour at a dosage of 3 lb acre and an exposure of 1 min under a drag sheet. Its predators, *Coccinella* and *Adalia*, with larvae of *Syrphus* and *Catabomba*, and its most important parasite, *Aphidius*, showed no mortality. The cabbage aphids that survived the fumigation were immediately killed by the predators, or by the parasites within the succeeding 3 weeks, so that their elimination was complete.[158] Orchard sprays of nicotine have no detrimental effect on the phytophagous mites and their mite and thrips predators, but they adversely influence the population of mirid predators [121a] (Table 7).

Pyrethrum, rotenone and BHC. The application of pyrethrum dusts to forests infested by the nun moth was found not to decrease the percentage of parasitism, and may even lead to an increase, e.g. to 96% as against 86% in the untreated area. The pyrethrum kills the caterpillars without killing the parasites within them. When the parasites emerge, they find an environment from which the chemically labile pyrethrins have disappeared.[71] On the other hand, rotenone decreased the parasitism. The use of rotenone-oil sprays to control *Icerya* scale on citrus had the effect of completely eradicating its coccinellid predator, *Rodolia cardinalis*.[40] Laboratory experiments have demonstrated that rotenone is toxic to all stages of coccinellids, although harmless to syrphid larvae.[188] The application of benzene hexachloride to control *Grapholitha* in peach orchards results in an increase of parasitism by *Macrocentrus* spp. to 45% as against 27% in the untreated plot.[157] The parasites on emergence find that the BHC has volatilized away. Field applications of BHC

have no adverse effect on predacious coccinellids.[140] Laboratory findings that BHC is sometimes toxic to coccinellids and highly toxic to *Aphidius* are open to reinterpretation for field conditions.[158] Nevertheless, the use of BHC on cotton has, like DDT, chlordane, and toxaphene, decidedly reduced the populations of coccinellids, *Geocoris*, and *Orius*, and caused infestations of *Tetranychus*. Its use has also resulted in the increase of *P. citri* on citrus.

The foregoing evidence emphasizes the fact that relatively indestructible insecticides like arsenicals, cryolite, and DDT are highly deleterious to the parasite population, since the adults are poisoned on coming in contact with them. Fumigants such as HCN, volatile insecticides such as nicotine, BHC, and parathion, and labile poisons such as pyrethrum and HETP do not affect the parasites, since they have decomposed or volatilized away by the time the adults emerge from their hosts. However, a successful attempt has been made to remove the residual contact effect of DDT to predators and parasites, and yet retain its stomach toxicity for defoliating pests, by including degraded cellulose in the formulation, which forms a protective coating over the DDT crystals. Residual films of this material did not kill the predator *Syrphus*, the parasite *Apanteles*, the honeybee, or the ant *Mormoniella*, whereas when sprayed on foliage it killed larvae of *Pieris* and *Tortrix*.[159]

D. Appearance of resistant strains of susceptible species

The San José scale (*Aspidiotus perniciosus*). A resistant strain was first observed in the Clarkston Valley, Washington, in 1908.[127] It showed approximately 17% survival to lime-sulphur sprays of a strength (2° Bé) that left no survivors of the normal strain of surrounding districts. Successive generations of this strain showed the same degree of resistance, there being no progressive increase thereof in 15 years.[128] A similar resistance was noted in the *Aspidiotus* of southern Illinois in 1920.[62] In both cases the resistant strain could be controlled by oil sprays, presumably as readily as the normal strain.

The black scale (*Saissetia oleae*). Scales unusually resistant to HCN fumigation were first noted at Charter Oak, California, in 1912.[198] By 1938 the phenomenon had spread through

Los Angeles County. The resistant strain showed 9–21% survival to concentrations of HCN (700 ppm)[155] that killed all but 1% of the normal stock. It can be controlled only by a dosage of HCN that is dangerous to the citrus tree.[75]

The California red scale (*Aonidiella aurantii*). Examples of a resistant strain were noted at Corona and Orange, California, between 1912 and 1914. By 1938 it was present in spots throughout the higher foothills around Los Angeles.[155] By 1946 it constituted a large part of the red scale population throughout the coast and interior of the region.[13] The resistant strain showed 8–19% survival to concentrations of HCN (3 cc/100 ft^3) that left only 1% of survivors of the normal strain.[151] In field practice the resistant strain showed 20% survival where 1% of the normal scales survived.[198]

The behaviour of the two strains showed a constant differential throughout 6 years (1935–41) of laboratory breeding.[202] Another investigation found the differential to be maintained for 70 generations.[115] Neither strains, however, were genetically homozygous with respect to resistance, since exposure to repeated fumigations could increase the resistance of either normal or resistant strain, a phenomenon observed originally in the field[151] and later confirmed in the laboratory.[202] The factor for resistance is sex-linked, the F_1 males resembling their mother in resistance, and is due to a gene or group of linked genes in the *X*-chromosome, which is diploid in the female and haploid in the male. Dominance is incomplete, since the heterozygous female (*Rr*) is intermediate in resistance between the normal strain (*rr*) and the resistant strain (*RR*). The proportion of resistant scales in the stock increases as the *r* males and the *rr* (and *rR*) females are progressively eliminated by the fumigation.[12]

No morphological difference is discernible between the two strains. Rates of development,[202] mortality rates at unfavourable temperatures, and reproductive ability proved to be identical.[135] However, scales of the resistant strain are able to achieve the state known as protective stupefaction (which results in an increased survival to killing doses of HCN) within 2 min of the application of initial sublethal dosages; on the other hand the normal strain takes 20 min to develop this refractory condition.[159] Moreover the resistant strain keeps its spiracles closed for 30 min

after the initial closure, which occurs 5 min after the administration of HCN; the non-resistant strain opens them 1 min after this closure.[82] A given application of HCN is "sorbed" to a greater amount in the bodies of the resistant than the non-resistant scales.[117]

The resistant strain also shows a greater degree of survival to fumigation with ethylene oxide or methyl bromide.[155] However, there was no difference from the normal strain in susceptibility to ethylene dibromide.[116] In spite of an impression gained in the field that the resistant strain showed higher survival to oil sprays than the normal,[155] systematic investigations showed the difference to be insignificant.[36, 115] However, there was a difference in response to cube resins, the resistant strain showing 6% survival to a concentration (0.013%) that allowed only 3% survival of the normal strain.[36] Oddly enough, the young adults of the resistant strain are more susceptible to methyl bromide than the normal strain, whereas the mature adults become more resistant than the normal strain.[201]

The citricola scale (*Coccus pseudomagnoliarum*). A highly cyanide-resistant strain of this species was first observed in 1925 near Riverside, California. By 1938 it occurred over the whole range of the species, in spite of virtual disappearance between 1934 and 1936. The resistance was such that 0.1% HCN controlled only 3–58% of this strain where normal stock showed 49–94% mortality.[155]

The citrus thrips (*Scirtothrips citri*). Two years after the introduction of tartar emetic (potassium antimony tartrate) for the control of this species, a decidedly resistant strain was discovered in the San Fernando Valley, California, in 1941. This strain showed 78% survival to deposits of tartar emetic (2.5μg/cm²) that allowed only 1% of the normal stock to survive.[22] In the field it resisted 4 times the usual dosage.[5] There is reason to suspect that a resistant strain of this species exists in certain areas of the western Transvaal.[165] By 1943, the gladiolus thrips *Taeniothrips simplex* had given evidence of resistance to tartar emetic in California.[170a] In the same year the walnut husk fly (*Rhagoletis completa*) of Southern California was noted to have a resistance to cryolite that it did not have 9 years before.[170]

The codling moth (*Carpocapsa pomonella*). The existence of a resistant strain in the Grand Valley of Colorado was realized by 1928, when as many as 10–12 cover sprays of acid lead arsenate were required to give the control afforded by 2 sprays annually in 1900. Spraying had been commenced about 1895 against the codling moth, which appeared in Colorado in 1891. The resistance was demonstrated experimentally in 1928 by comparison with a strain of codling moth from the Shenandoah Valley, Virginia, where only 4 cover sprays were required annually.[92] The Colorado larvae were found to grow larger than the Virginia strain, and to maintain their greater resistance to acid lead arsenate sprays when grown in Virginia orchards among the native strain. They showed a greater ability to enter fruit, whether sprayed or unsprayed. Their distinction was not due to a resistance to ingested arsenate or to a greater boring ability. The Colorado strain showed as much susceptibility as Virginia or Missouri strains to lead arsenate or sodium arsenite ingested or injected.[82a] But it did differ in its capacity to survive many unsuccessful stings, being repulsed by the poison, and still proceed to find a point of entry into the apple. For this advantage, the resistant larvae were endowed with a greater ability to maintain their body weight against desiccation or starvation. This increase in resistance to the environment allowed them more time and opportunity to find entrance. They also showed an enhanced resistance to deposits of cryolite, barium fluosilicate, or rotenone on apples.[95]

A cross of the Colorado with the Virginia strain gave an F_1 hybrid showing intermediate resistance.[93] Identical results were obtained by the reciprocal cross,[94] indicating that the factor was not sex-linked. The hybrids maintained their intermediate position when bred for 9 further generations. A back-cross of the hybrid with either the Colorado or Virginia strain gave progeny intermediate between the hybrid and the respective parent strain. At the same time, the strain of codling moth in the Yakima Valley, Washington, was found to be comparable in resistance to the original hybrid strain.[94] Evidence of selection proceeding in this interior Washington stock was obtained at Wenatchee, where a given deposit of lead arsenate (60 μg in.$^{-2}$) controlled only 36% of field-collected larvae in 1932, as against 60% in

1931 and 73% in 1930.[190] In Indiana, larvae from an orchard unsprayed for 6 years were considerably less able to enter sprayed fruit than larvae from an orchard which had continually been sprayed with lead arsenate. Even in Virginia, the codling moth has required over twice the amount of spraying with lead arsenate to achieve a given control in 1943 as it did in 1918.[96] By 1943 there was evidence of increased resistance to basic lead arsenate of the codling moth infesting walnuts in California.[156a]

The peach twig borer (*Anarsia lineatella*). A strain showing resistance to basic lead arsenate was discovered in 1944 in a small area near Empire, California, where the usual 2 cover sprays were followed with fruit losses of 20–50%. Laboratory examination of this strain showed that 20% of the larvae could penetrate coatings from 0.4% lead arsenate and establish themselves in the peach, whereas only 3% of the normal strain could do so.[173]

The blue tick (*Boophilus decoloratus*). A strain of this cattle tick that was resistant to sodium arsenite dips was first discovered near East London, Cape Province, South Africa, in 1938. By 1940 it occurred for a distance of about 80 miles along the coast, and by 1945 had spread south to the Alexandria district and north to Zululand.[193] Of the resistant strain, 63% survived to lay eggs after a dip (0.64% As_2O_3) which allowed only 1% of the normal strain to survive and lay.[142] Other concomitant species of cattle ticks, *Rhipicephalus* spp. and *Amblyomma*, in this area did not show resistance.[18] The resistant *Boophilus* were not controlled by concentrations so high as to endanger the cattle. It has been the general experience that resistance to arsenite dips has developed in the *Boophilus australis* of Australia[2] and the *Haematobia hominis* of Brazil.

The greenhouse red spider (*Tetranychus telarius*). A strain of this mite that was resistant to parathion was discovered in 1949 in a greenhouse at Cromwell, Connecticut.[63b] The resistance was such that a concentration of parathion sufficient to kill 100% of the normal strain caused only 15% mortality of the resistant strain. This strain showed little or no resistance to DMC or DCPM, although there was some evidence that it could

build up resistance to TEPP in time. Mites resistant to parathion and other acaricides appear on greenhouse roses rather than other plants.[135b] Greenhouse red spider resistant to selenium (*Selocide*) had appeared in the Eastern States by 1943.[156a]

Other laboratory-selected strains. A laboratory stock of the flour beetle (*Tribolium confusum*) was found to be readily divisible on the basis of resistance to HCN fumigation. The offspring of those spent adults that constituted the survivors of a subsequent fumigation were found to require an LC_{50} that was 60% higher than the offspring of those adults that were the victims of the HCN fumigation. The resistant group had a higher oxygen uptake (2.8 versus 2.2 cu mm/mg), but was not morphologically different.[72] By artificial selection over 7 generations, strains of the vinegar fly (*Drosophila melanogaster*) and the cotton aphid (*Aphis gossypii*) were obtained which showed slightly increased resistance to HCN fumigation. A strain of the screwworm (*Cochliomyia americana*) was developed by breeding the larvae in 0.10% phenothiazine for 8 generations. This strain developed such resistance that only 3% were killed in a concentration of 0.17% phenothiazine that killed 66% of the normal stock. The resistant stock, however, was as susceptible as the normal to diphenylamine or diphenylene oxide, compounds structurally related to phenothiazine.[106]

Strains of the housefly (*Musca domestica*) whose adults are resistant to certain chlorinated hydrocarbons have evolved as readily as DDT-resistant strains. A stock that had been bred in a BHC-contaminated laboratory for 28 generations showed only 6% mortality to a level of lindane that had killed 40% of its unexposed forefathers.* This strain also showed a greater resistance than normal strains to DDT, pyrethrins, and *Lethane 384 Special*, but this resistance was not as marked as that to lindane.[15] Another strain, developed in the laboratory by exposure of the larvae and adults to lindane, gradually developed a resistance to lindane, chlordane, toxaphene, and dieldrin, but not to DDT.[24a] Houseflies bred in a chlordane plant at Denver

* A field strain resistant to BHC has been collected from the Pollard ranch, Santa Ana, Calif., where BHC had been applied during the preceding 5 months.[183a]

show enhanced resistance to chlordane, but a lesser increase of resistance to other chemicals.[123] On the other hand, it proved impossible to develop strains resistant to chlordane or to toxaphene by laboratory selection.[24a] By repeated treatment of larvae and adults with the respective insecticides, strains showing tolerance for dieldrin, para-oxon, and pyrethrins were developed. The strain resistant to pyrethrins (plus piperonyl butoxide) proved to be generally tolerant of all insecticides.[24a]

It is probable that insect species sufficiently abundant to be economic pests are in nature heterozygous for many genes. For example, 31 lines of the pea aphid (*Macrosiphum pisi*) collected from various parts of the United States were found to fall into 5 biological races on the basis of size, reproductive rates, and feeding damage.[83] They thus offer a range of genotypes from which the application of insecticides may select the more resistant ones. Because of the high biotic potential of insects this process may take place with considerable rapidity. It is also possible that new mutant genes may appear during the period over which chemical control has been practiced (*Anarsia* has been suggested as an example); but it would require a long period of time for them to spread sufficiently to constitute a large element in the population. The direct acquisition of resistance in response to the insecticide, or cytoplasmic modification, is unlikely to be an important factor. The reversion of resistant strains when reared free of the insecticide, as found in some cases of DDT-resistant flies, may be due to a residual heterozygosity in the resistant stock, and need not point to a cytoplasmic origin of the resistance.

It may well be asked why resistance to insecticides has not occurred more frequently among the wide variety of economic insects. It has been pointed out as a principal reason that the resistant surviving stock in areas of control may have been submerged by breeding with the population of the surrounding insecticide-free area. Indeed, resistance has occurred more commonly with sedentary species such as the coccids. Another factor may be that the acquisition of resistance involves some other characteristic that may be a handicap for survival, e.g. lessened fertility in the arsenic-resistant *Carpocapsa*.[132a]

Any insect population exhibits variation in susceptibility to insecticides according to a normal frequency distribution, and upon this assumption the concept of the median lethal dosage is based. Klinger observed that a group of caterpillars of any one species showed a proportion of resistant plus-variants and susceptible minus-variants when tested with an insecticide such as pyrethrum, and that these variants decreased in proportion as the larvae increased in age. He pointed out that these variants may be genotypic, due to their hereditary constitution, or phenotypic, dependent on their material or maternal nourishment.[105] When so-called resistant strains are encountered it is necessary to distinguish between resistance induced by conditions of growth and resistance fixed from generation to generation.

TABLE 8. Effect of Food Medium on the Susceptibility of *Culex* Larvae to Insecticides[148]

Percentage mortality in fresh water containing the insecticide

Food Medium	Rotenone, 5 ppm	Nicotine, 100 ppm
Hay infusion 100%	15	18
Hay infusion 50%	59	75
Hay infusion 5%	91	97
Yeast and blood 2%	35	23
Yeast and blood 0.1%	57	64
Yeast and blood 0.05%	90	87

That larval nourishment has an effect upon the resistance of insects to insecticides has been experimentally demonstrated with *Culex quinquefasciatus* and *Musca domestica*. The dilution of a hay infusion 20 times was found to increase the mortality of the mosquito larvae reared in it, on exposure to given doses of rotenone or nicotine, from 15 to 18% up to 91 and 97%, respectively (Table 8). A similar dilution of chow feed from 0.25% down to 0.05% increased the susceptibility of these larvae to DDT from 42% up to 81%.[148] The type of nutrition given adult houseflies can affect their susceptibility to sprays containing DDT or pyrethrum, a diet of dried whey powder inducing them to show 70% mortality to doses that cause only 40% kill when the flies have been fed on fresh skimmed milk.[125]

QUANTITATIVE ASPECTS OF VARIABILITY IN RESISTANCE

Any population of insects will be found to show a range of variation in their susceptibility to insecticides. This variation may be decreaesd by uniform conditions of rearing, but there still remains an irreducible minimum of variation due mainly to genetic causes. Thus there is a considerable range of dosage between the threshold figure where no mortality occurs, and the dosage where 100% mortality is obtained. Quantitative assessment of toxicity of an insecticide is based on a study of percentage mortality in this range.*

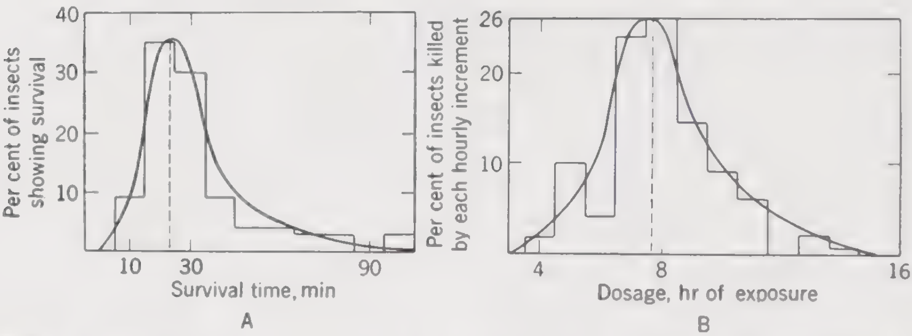

FIG. 2. Frequency distribution of susceptibility of insect populations. A Survival times of *Periplaneta* to injections of sodium arsenite. (From Yeager and Munson) B. Dosage increment classes of *Tribolium* exposed to hot dry air. (From Shepard)

The frequency distribution of the susceptibilities of the individual members of an insect population cannot be derived directly because it is impossible to establish the minimum lethal dose for each individual member. However, some indication of the type of "normal curve" to be expected may be obtained from a study of the survival times of individuals to a given dosage (Fig. 2A). It is seen that the distribution is asymmetrical, with a much wider range of variation among the resistant individuals

* Corrected for control mortality by Abbott's formula [*J. Econ. Ent.*, **18**:65 (1925)], to equal $\frac{x-y}{x} \times 100$, where x is the per cent survival in the untreated control, and y is the percent survival in the treated experimental sample.

than among the susceptible ones. The same skewed curve is shown when the number of insects falling into each class succumbing to each unit increment of dosage is plotted against the dosage (Fig. 2B). Since the progression minimum → median → maximum is geometrical rather than arithmetical, the curves become symmetrical if the values on the abscissa are plotted on a logarithmic scale.

Similarly when these values are plotted cumulatively on a dosage-mortality graph, the resulting sigmoid curve is asymmetrical when the dosage is plotted arithmetically on the abscissa, because of the very much larger dosage increments which are required to kill the most resistant individuals in the population (Fig. 3A). This asymmetry disappears if the dosage is plotted on a logarithmic scale (Fig. 3B). It has been observed in many physiological processes that equal increments in effect are produced only when the stimulus is increased by a constant *proportion* of a given dosage, rather than by a constant *amount*.[15a]

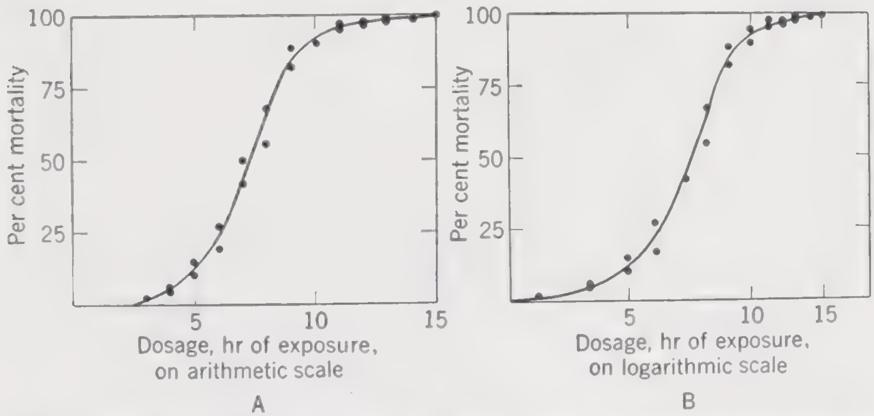

FIG. 3. Dosage-mortality curves for *Tribolium* exposed to hot dry air. (From Shepard) A. Asymmetrical sigmoid curve, with dosage on arithmetic scale. B. Symmetrical sigmoid curve, with dosage on logarithmic scale.

The toxicity of the insecticide under study may then be expressed in terms of the median lethal dosage or LD_{50}, that dosage at which 50% of the insect population is susceptible enough to succumb and 50% is sufficiently resistant to survive. But the economic entomologist is more interested in the dosage figure that kills all or nearly all of the population, e.g. the LD_{90}, and

he would be interested in the LD_{50} figure if the results at higher dosages and higher mortalities were given equal weight in establishing that figure. Hence a method has been developed to transform the dosage-mortality relationship from a sigmoid curve into a straight line. This is effected either by plotting the percentage mortality on a probability scale, using logarithm-probability graph paper;[139a] or by transforming the mortality values into probability units and plotting them arithmetically against log dosage (Fig. 4). The "probit" (probability unit) corresponding

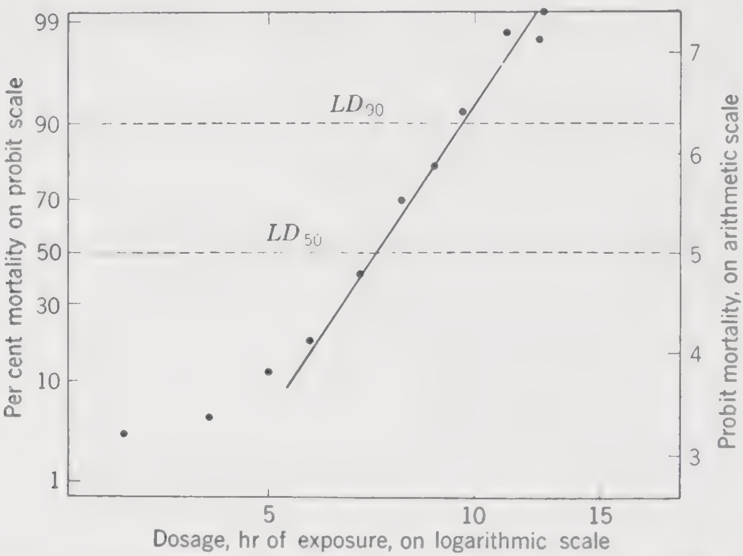

FIG. 4. Dosage-mortality curves for *Tribolium* exposed to hot dry air (From Shepard) Linear relationship between probit mortality and log dosage.

to 50% mortality is arbitrarily given the value of 5.0, and the values in either direction are then calculated in a symmetrical manner.[15a] Tables of calculated probits have been published by Bliss (Table 9), and graph paper is available with both probit and probability scales.* One of the advantages of arithmetic probits is that they allow the straight line to be statistically fitted by the method of least squares. However, nomographs have been prepared which allow the statistical fitting of a line to values directly plotted on logarithm-probability paper.[139a] It will be found that the slopes of the dosage-mortality relationship

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TABLE 9. PROBITS OR PROBABILITY UNITS FOR TRANSFORMING THE SIGMOID DOSAGE-MORTALITY CURVE TO A STRAIGHT LINE

In the body of the table is given the probit corresponding to each percentage mortality listed along the left edge and top. (From Bliss, courtesy of *Annals of Applied Biology*)

	0.0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9
0	. . .	1.9098	2.1218	2.2522	2.3479	2.4242	2.4879	2.5427	2.5911	2.6344
1	2.6737	2.7096	2.7429	2.7738	2.8027	2.8299	2.8556	2.8799	2.9031	2.9251
2	2.9463	2.9665	2.9859	3.0046	3.0226	3.0400	3.0569	3.0732	3.0890	3.1043
3	3.1192	3.1337	3.1478	3.1616	3.1750	3.1881	3.2009	3.2134	3.2256	3.2376
4	3.2493	3.2608	3.2721	3.2831	3.2940	3.3046	3.3151	3.3253	3.3354	3.3454
5	3.3551	3.3648	3.3742	3.3836	3.3928	3.4018	3.4107	3.4195	3.4282	3.4368
6	3.4452	3.4536	3.4618	3.4699	3.4780	3.4859	3.4937	3.5015	3.5091	3.5167
7	3.5242	3.5316	3.5389	3.5462	3.5534	3.5605	3.5675	3.5745	3.5813	3.5882
8	3.5949	3.6016	3.6083	3.6148	3.6213	3.6278	3.6342	3.6405	3.6468	3.6531
9	3.6592	3.6654	3.6715	3.6775	3.6835	3.6894	3.6953	3.7012	3.7070	3.7127
10	3.7184	3.7241	3.7298	3.7354	3.7409	3.7464	3.7519	3.7574	3.7628	3.7681
11	3.7735	3.7788	3.7840	3.7893	3.7945	3.7996	3.8048	3.8099	3.8150	3.8200
12	3.8250	3.8300	3.8350	3.8399	3.8448	3.8497	3.8545	3.8593	3.8641	3.8689
13	3.8736	3.8783	3.8830	3.8877	3.8923	3.8969	3.9015	3.9061	3.9107	3.9152
14	3.9197	3.9242	3.9286	3.9331	3.9375	3.9419	3.9463	3.9506	3.9550	3.9593
15	3.9636	3.9678	3.9721	3.9763	3.9806	3.9848	3.9890	3.9931	3.9973	4.0014
16	4.0055	4.0096	4.0137	4.0178	4.0218	4.0259	4.0299	4.0339	4.0379	4.0419
17	4.0458	4.0498	4.0537	4.0576	4.0615	4.0654	4.0693	4.0731	4.0770	4.0808
18	4.0846	4.0884	4.0922	4.0960	4.0998	4.1035	4.1073	4.1110	4.1147	4.1184
19	4.1221	4.1258	4.1295	4.1331	4.1367	4.1404	4.1440	4.1476	4.1512	4.1548
20	4.1584	4.1619	4.1655	4.1690	4.1726	4.1761	4.1796	4.1831	4.1866	4.1901
21	4.1936	4.1970	4.2005	4.2039	4.2074	4.2108	4.2142	4.2176	4.2210	4.2244
22	4.2278	4.2312	4.2345	4.2379	4.2412	4.2446	4.2479	4.2512	4.2546	4.2579
23	4.2612	4.2644	4.2677	4.2710	4.2743	4.2775	4.2808	4.2840	4.2872	4.2905
24	4.2937	4.2969	4.3001	4.3033	4.3065	4.3097	4.3129	4.3160	4.3192	4.3224
25	4.3255	4.3287	4.3318	4.3349	4.3380	4.3412	4.3443	4.3474	4.3505	4.3536
26	4.3567	4.3597	4.3628	4.3659	4.3689	4.3720	4.3750	4.3781	4.3811	4.3842
27	4.3872	4.3902	4.3932	4.3962	4.3992	4.4022	4.4052	4.4082	4.4112	4.4142
28	4.4172	4.4201	4.4231	4.4260	4.4290	4.4319	4.4349	4.4378	4.4408	4.4437
29	4.4466	4.4495	4.4524	4.4554	4.4583	4.4612	4.4641	4.4670	4.4698	4.4727
30	4.4756	4.4785	4.4813	4.4842	4.4871	4.4899	4.4928	4.4956	4.4985	4.5013
31	4.5041	4.5070	4.5098	4.5126	4.5155	4.5183	4.5211	4.5239	4.5267	4.5295
32	4.5323	4.5351	4.5379	4.5407	4.5435	4.5462	4.5490	4.5518	4.5546	4.5573
33	4.5601	4.5628	4.5656	4.5684	4.5711	4.5739	4.5766	4.5793	4.5821	4.5848
34	4.5875	4.5903	4.5930	4.5957	4.5984	4.6011	4.6039	4.6066	4.6093	4.6120
35	4.6147	4.6174	4.6201	4.6228	4.6255	4.6281	4.6308	4.6335	4.6362	4.6389
36	4.6415	4.6442	4.6469	4.6495	4.6522	4.6549	4.6575	4.6602	4.6628	4.6655
37	4.6681	4.6708	4.6734	4.6761	4.6787	4.6814	4.6840	4.6866	4.6893	4.6919
38	4.6945	4.6971	4.6998	4.7024	4.7050	4.7076	4.7102	4.7129	4.7155	4.7181
39	4.7207	4.7233	4.7259	4.7285	4.7311	4.7337	4.7363	4.7389	4.7415	4.7441
40	4.7467	4.7492	4.7518	4.7544	4.7570	4.7596	4.7622	4.7647	4.7673	4.7699
41	4.7725	4.7750	4.7776	4.7802	4.7827	4.7853	4.7879	4.7904	4.7930	4.7955
42	4.7981	4.8007	4.8032	4.8058	4.8083	4.8109	4.8134	4.8160	4.8185	4.8211
43	4.8236	4.8262	4.8287	4.8313	4.8338	4.8363	4.8389	4.8414	4.8440	4.8465
44	4.8490	4.8516	4.8541	4.8566	4.8592	4.8617	4.8642	4.8668	4.8693	4.8718
45	4.8743	4.8769	4.8794	4.8819	4.8844	4.8870	4.8895	4.8920	4.8945	4.8970
46	4.8996	4.9021	4.9046	4.9071	4.9096	4.9122	4.9147	4.9172	4.9197	4.9222
47	4.9247	4.9272	4.9298	4.9323	4.9348	4.9373	4.9398	4.9423	4.9448	4.9473
48	4.9498	4.9524	4.9549	4.9574	4.9599	4.9624	4.9649	4.9674	4.9699	4.9724
49	4.9749	4.9774	4.9799	4.9825	4.9850	4.9875	4.9900	4.9925	4.9950	4.9975

[*Continued on p. 768.*]

TABLE 9. PROBITS OR PROBABILITY UNITS FOR TRANSFORMING THE SIGMOID DOSAGE-MORTALITY CURVE TO A STRAIGHT LINE.—*Continued*

In the body of the table is given the probit corresponding to each percentage mortality listed along the left edge and top. (From Bliss, courtesy of *Annals of Applied Biology*)

	0.0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9
50	5.0000	5.0025	5.0050	5.0075	5.0100	5.0125	5.0150	5.0175	5.0201	5.0226
51	5.0251	5.0276	5.0301	5.0326	5.0351	5.0376	5.0401	5.0426	5.0451	5.0476
52	5.0502	5.0527	5.0552	5.0577	5.0602	5.0627	5.0652	5.0677	5.0702	5.0728
53	5.0753	5.0778	5.0803	5.0828	5.0853	5.0878	5.0904	5.0929	5.0954	5.0979
54	5.1004	5.1030	5.1055	5.1080	5.1105	5.1130	5.1156	5.1181	5.1206	5.1231
55	5.1257	5.1282	5.1307	5.1332	5.1358	5.1383	5.1408	5.1434	5.1459	5.1484
56	5.1510	5.1535	5.1560	5.1586	5.1611	5.1637	5.1662	5.1687	5.1713	5.1738
57	5.1764	5.1789	5.1815	5.1840	5.1866	5.1891	5.1917	5.1942	5.1968	5.1993
58	5.2019	5.2045	5.2070	5.2096	5.2121	5.2147	5.2173	5.2198	5.2224	5.2250
59	5.2275	5.2301	5.2327	5.2353	5.2378	5.2404	5.2430	5.2456	5.2482	5.2508
60	5.2533	5.2559	5.2585	5.2611	5.2637	5.2663	5.2689	5.2715	5.2741	5.2767
61	5.2793	5.2819	5.2845	5.2871	5.2898	5.2924	5.2950	5.2976	5.3002	5.3029
62	5.3055	5.3081	5.3107	5.3134	5.3160	5.3186	5.3213	5.3239	5.3266	5.3292
63	5.3319	5.3345	5.3372	5.3398	5.3425	5.3451	5.3478	5.3505	5.3531	5.3558
64	5.3585	5.3611	5.3638	5.3665	5.3692	5.3719	5.3745	5.3772	5.3799	5.3826
65	5.3853	5.3880	5.3907	5.3934	5.3961	5.3989	5.4016	5.4043	5.4070	5.4097
66	5.4125	5.4152	5.4179	5.4207	5.4234	5.4261	5.4289	5.4316	5.4344	5.4379
67	5.4399	5.4427	5.4454	5.4482	5.4510	5.4538	5.4565	5.4593	5.4621	5.4642
68	5.4677	5.4705	5.4733	5.4761	5.4789	5.4817	5.4845	5.4874	5.4902	5.4930
69	5.4959	5.4987	5.5015	5.5044	5.5072	5.5101	5.5129	5.5158	5.5187	5.5215
70	5.5244	5.5273	5.5302	5.5330	5.5359	5.5388	5.5417	5.5446	5.5476	5.5505
71	5.5534	5.5563	5.5592	5.5622	5.5651	5.5681	5.5710	5.5740	5.5769	5.5799
72	5.5828	5.5858	5.5888	5.5918	5.5948	5.5978	5.6008	5.6038	5.6068	5.6098
73	5.6128	5.6158	5.6189	5.6219	5.6250	5.6280	5.6311	5.6341	5.6372	5.6403
74	5.6433	5.6464	5.6495	5.6526	5.6557	5.6588	5.6620	5.6651	5.6682	5.6713
75	5.6745	5.6776	5.6808	5.6840	5.6871	5.6903	5.6935	5.6967	5.6999	5.7031
76	5.7063	5.7095	5.7128	5.7160	5.7192	5.7225	5.7257	5.7290	5.7323	5.7356
77	5.7388	5.7421	5.7454	5.7488	5.7521	5.7554	5.7588	5.7621	5.7655	5.7688
78	5.7722	5.7756	5.7790	5.7824	5.7858	5.7892	5.7926	5.7961	5.7995	5.8030
79	5.8064	5.8099	5.8134	5.8169	5.8204	5.8239	5.8274	5.8310	5.8345	5.8381
80	5.8416	5.8452	5.8488	5.8524	5.8560	5.8596	5.8633	5.8669	5.8705	5.8742
81	5.8779	5.8816	5.8853	5.8890	5.8927	5.8965	5.9002	5.9040	5.9078	5.9116
82	5.9154	5.9192	5.9230	5.9269	5.9307	5.9346	5.9385	5.9424	5.9463	5.9502
83	5.9542	5.9581	5.9621	5.9661	5.9701	5.9741	5.9782	5.9822	5.9863	5.9904
84	5.9945	5.9986	6.0027	6.0069	6.0110	6.0152	6.0194	6.0237	6.0279	6.0322
85	6.0364	6.0407	6.0450	6.0494	6.0537	6.0581	6.0625	6.0669	6.0714	6.0758
86	6.0803	6.0848	6.0893	6.0939	6.0985	6.1031	6.1077	6.1123	6.1170	6.1217
87	6.1264	6.1311	6.1359	6.1407	6.1455	6.1503	6.1552	6.1601	6.1650	6.1700
88	6.1750	6.1800	6.1850	6.1901	6.1952	6.2004	6.2055	6.2107	6.2160	6.2212
89	6.2265	6.2319	6.2372	6.2426	6.2481	6.2536	6.2591	6.2646	6.2702	6.2759
90	6.2816	6.2873	6.2930	6.2988	6.3047	6.3106	6.3165	6.3225	6.3285	6.3346
91	6.3408	6.3469	6.3532	6.3595	6.3658	6.3722	6.3787	6.3852	6.3917	6.3984
92	6.4051	6.4118	6.4187	6.4255	6.4325	6.4395	6.4466	6.4538	6.4611	6.4684
93	6.4758	6.4833	6.4909	6.4985	6.5063	6.5141	6.5220	6.5301	6.5382	6.5464
94	6.5548	6.5632	6.5718	6.5805	6.5893	6.5982	6.6072	6.6164	6.6258	6.6352
95	6.6449	6.6546	6.6646	6.6747	6.6849	6.6954	6.7060	6.7169	6.7279	6.7392
96	6.7507	6.7624	6.7744	6.7866	6.7991	6.8119	6.8250	6.8384	6.8522	6.8663
97	6.8808	6.8957	6.9110	6.9268	6.9431	6.9600	6.9774	6.9954	7.0141	7.0335

TABLE 9. PROBITS OR PROBABILITY UNITS FOR TRANSFORMING THE SIGMOID DOSAGE-MORTALITY CURVE TO A STRAIGHT LINE.—*Continued*

In the body of the table is given the probit corresponding to each percentage mortality listed along the left edge and top. (From Bliss, courtesy of *Annals of Applied Biology*)

	0.00	0.01	0.02	0.03	0.04	0.05	0.06	0.07	0.08	0.09
98.0	7.0537	7.0558	7.0579	7.0600	7.0621	7.0642	7.0663	7.0684	7.0706	7.0727
98.1	7.0749	7.0770	7.0792	7.0814	7.0836	7.0858	7.0880	7.0902	7.0924	7.0947
98.2	7.0969	7.0992	7.1015	7.1038	7.1060	7.1084	7.1107	7.1130	7.1154	7.1177
98.3	7.1201	7.1224	7.1248	7.1272	7.1297	7.1321	7.1345	7.1370	7.1394	7.1419
98.4	7.1444	7.1469	7.1494	7.1520	7.1545	7.1571	7.1596	7.1622	7.1648	7.1675
98.5	7.1701	7.1727	7.1754	7.1781	7.1808	7.1835	7.1862	7.1890	7.1917	7.1945
98.6	7.1973	7.2001	7.2029	7.2058	7.2086	7.2115	7.2144	7.2173	7.2203	7.2232
98.7	7.2262	7.2292	7.2322	7.2353	7.2383	7.2414	7.2445	7.2476	7.2508	7.2539
98.8	7.2571	7.2603	7.2636	7.2668	7.2701	7.2734	7.2768	7.2801	7.2835	7.2869
98.9	7.2904	7.2938	7.2973	7.3009	7.3044	7.3080	7.3116	7.3152	7.3189	7.3226
99.0	7.3263	7.3301	7.3339	7.3378	7.3416	7.3455	7.3495	7.3535	7.3575	7.3615
99.1	7.3656	7.3698	7.3739	7.3781	7.3824	7.3867	7.3911	7.3954	7.3999	7.4044
99.2	7.4089	7.4135	7.4181	7.4228	7.4276	7.4324	7.4372	7.4422	7.4471	7.4522
99.3	7.4573	7.4624	7.4677	7.4730	7.4783	7.4838	7.4893	7.4949	7.5005	7.5063
99.4	7.5121	7.5181	7.5241	7.5302	7.5364	7.5427	7.5491	7.5556	7.5622	7.5690
99.5	7.5758	7.5828	7.5899	7.5972	7.6045	7.6121	7.6197	7.6276	7.6356	7.6437
99.6	7.6521	7.6606	7.6693	7.6783	7.6874	7.6968	7.7065	7.7164	7.7265	7.7370
99.7	7.7478	7.7589	7.7703	7.7821	7.7944	7.8070	7.8202	7.8338	7.8480	7.8627
99.8	7.8782	7.8943	7.9112	7.9291	7.9478	7.9677	7.9889	8.0114	8.1357	8.0618
99.9	8.0902	8.1214	8.1559	8.1947	8.2389	8.2905	8.3528	8.4316	8.5401	8.7190

vary according to the insecticide, those for DDT and its analogues being characteristically shallow and long drawn out, while those for fumigants are typically steep (i.e. little range in dosage between the LD_{90} and the LD_{50}).

Values for the LD_{50} or LD_{90} are ideally expressed in micrograms per gram of insect weight, which is synonymous with the milligrams per kilogram unit. In the case of injected insecticides and some stomach poisons the figures have been directly determined. Dosages of contact and residual insecticides may be measured in terms of micrograms deposited per square centimetre (1 μg/cm^2 is approximately equivalent to 0.09 lb/acre). More frequently, however, these dosages are measured in terms of concentration of the spray. Fumigant doses in air are expressed as milligrams per litre for a given time, and dissolved insecticides in water may be similarly expressed in parts per million. Alternatively the time factor may be taken into account and the dosage expressed as the Ct figure in terms of mg-min/m^3. However, the Ct (the product of concentration and exposure

time) is not constant for all values of C and t, being higher when they are at the extremes, and reaching a minimum on a point somewhere on the arch between them.[65] Since the LD_{50} value varies inversely as the toxicity, the index of toxicity for comparative purposes should be based on the reciprocal of the LD_{50} value; or rather, since the lethal effect is more closely correlated with log dosage, it should be based on the reciprocal of the logarithm of the LD_{50} value.

For the specialized field of the application of statistics to toxicology, the reader is referred to the chapters by Shepard [164a] and by Wadley [185a] and to Snedecor's book.[168a]

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